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THE

AMERICAN JOURNAL
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JUNE, 1913

ORIGINAL ARTICLES

CLINICAL OBSERVATIONS CONCERNING TWENTY-SEVEN CASES OF SPLENECTOMY.[1]

By H. Z. Giffin, M.D.,

ATTENDING PHYSICIAN TO ST. MARY'S HOSPITAL, MAYO CLINIC, ROCHESTER, MINNESOTA.

The association of enlarged spleen with anemia occurs in so many diseases and in such a variety of abdominal conditions that a fuller knowledge will be necessary before one can arrive at a correct classification of splenomegaly. The results of medical, surgical, pathological, and experimental experience must be reported abundantly before a correct grouping can be even attempted.

That a certain picture conforming to splenic anemia as it is clinically described presents itself there is, of course, no doubt. However, the many factors that are discussed by writers on the etiology of this condition at once make one question the advisability of stamping a given case with a certain stencil. Syphilis, malaria, passive congestion as a result of portal obstruction, thrombosis of the splenic or portal veins, the occurrence of Leischmann-Donovan bodies, the action of extraneous toxins, the occurrence of hemolysis, the existence of an undemonstrated infectious agent —these have all been considered as factors in the causation of certain cases. And there must be added to this list, after a consideration of the cases herewith reviewed, what appears to be more than an accidental association of disease of the gall-bladder, with cases that can properly be diagnosticated clinically as splenic anemia. Moreover, at one extreme, there are many histories of short duration or those without the typical symptomatology and cases with atypical blood count, while at the other extreme there are instances in which cirrhosis of the liver seems to form a slightly

[1] Read before the Mississippi Valley Medical Association, Chicago, October 22 to 24, 1912.

more prominent part of the picture than the changes in the spleen. And apart from the clinical and etiological aspects there is confusion on the pathological side. The examination of spleens removed from patients regarded from the clinical standpoint as cases of typical splenic anemia reveals no constant histologic picture. Connective-tissue increase is the common finding, but endothelial or lymphocytic hyperplasia may predominate to such a degree that the picture may even simulate a true tumor.

Where then shall the line be drawn in determining the degree of variation permissible in the cases we are to regard as splenic anemia? However, without entering further into the general discussion of conditions simulating splenic anemia, it is my purpose to present the clinical findings in those cases in which splenectomy has been done in the Mayo clinic.

The total number of splenectomies from April 6, 1904, to July 5, 1912, is 27. For convenience these are divided into three groups: (1) Those which conform closely to the clinical syndrome of splenic anemia, 18 in number; (2) cases presenting clinical features which suggest that the splenomegaly was a part of a more or less widespread infection and secondary rather than primary; (3) miscellaneous cases.

GROUP I. Splenic anemia (18 cases). Splenic anemia is at present a clinical entity. Therefore in selecting cases for this group the preoperative clinical picture was relied upon. A great and apparently uncomplicated increase in the size of the spleen and an anemia of the secondary type, usually with leukopenia, have been considered essential in the diagnosis. Where the clinical picture was complicated by any condition which would lead one to consider the splenomegaly as a secondary rather than a primary process, and likewise when the surgical pathology was definitely that of some other condition, the case was excluded. Two cases in which the spleen showed a predominating lymphocytic hyperplasia and three presenting an endothelial hyperplasia are grouped as splenic anemia because of their clinical course, and also for the reason that pathologists have not definitely decided that these conditions represent any thing more than different types of reaction.

Twelve of the patients were females and 6 males. The youngest patient was aged twenty-two years, and the oldest fifty-six years. The average age was thirty-seven years. The distribution as to decades was as follows: Between twenty and thirty years, 6; between thirty and forty years, 4; between forty and fifty years, 5; between fifty and sixty years, 3.

Enlargement of the spleen was noted in one case twenty years before operation; in another case fifteen years; in a third ten years. In 8 instances splenic enlargement had been noted less than a year preceding operation, and in the remaining 7 from one to seven years. It is probable, however, that splenomegaly had in reality been present for a longer time in many of these cases. In

14 of the 18 cases the enlargement of the spleen had definitely preceded the appearance of anemia. In no case did the occurrence of anemia clearly precede splenomegaly.

The recorded measurements of all the spleens of this group show them to be either large or enormous in size. The average length of the spleens in the 18 cases was 24 cm. All of them save 1, which lay transversely, reached below the level of the navel, and 7 extended into the left iliac fossa and beyond the median line. The largest spleen weighed 5280 grams, the smallest 425 grams. The weight was recorded in each instance; the average weight was 1680 grams. In none of them did the long axis extend diagonally across the abdomen, but lay almost entirely to the left of the median line. It is interesting to note that one spleen lay very high and the enlargement extended transversely into the epigastrium, only one-eighth of the spleen being palpable below the costal margin.

In 4 instances the contour of the spleen was not outlined definitely enough to warrant a diagnosis without the aid of a cystoscopic examination, and in 1 of these a colloidal silver radiograph was necessary to demonstrate a normal kidney pelvis. Indeed, it may be impossible to diagnosticate an abdominal tumor positively as a spleen without these procedures.

There was nothing typical about the blood in these cases save that the anemia was of the secondary type, and there was an absence of leukocytosis. The count made within a few days of operation in each case showed a hemoglobin percentage below 75 per cent. in all instances save 3; in these there had been a preceding anemia. In most of the cases an attempt had been previously made to improve the condition of the blood before operation was undertaken. In 1 the hemoglobin had been as low as 20 per cent., in another, 35 per cent. In 10 the hemoglobin had been below 50 per cent.

In 12 instances the leukocyte count was below 5500; in 1, as low as 1000. In only 1 case was a high count obtained (11,000), and this patient had been under the observation of William Osler, who regarded the condition as splenic anemia. The average of the remaining 17 cases was 4200. The occurrence of leukocytosis after operation as noted by other observers is corroborated in this series. Pain in the long bones was complained of by several patients after operation.

Differential counts were not distinctly abnormal, save that an occasional normoblast and megaloblast were found. The reader is referred to the accompanying blood chart for a more detailed conception of the findings.

Hematemesis occurred in 5 of the 18 cases; in 4 of these it was severe. In 1 case it had occurred every year for fifteen years. Blood in the bowel movement was also present at these times. In 1 case of Banti's disease, in which hematemesis had been severe

for nine months, the hemoglobin dropped as low as 20 per cent. This patient has been well for three and a half years following the operation. Another patient had had four attacks of bleeding

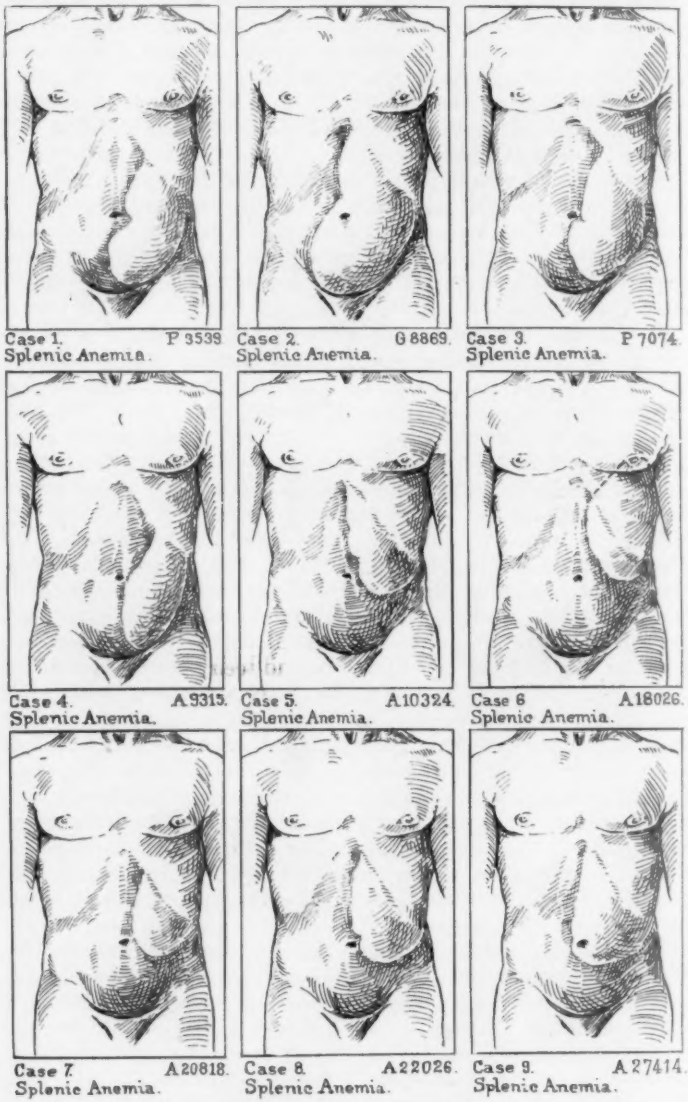

FIG. 1.—Contour and position of spleen as observed clinically before operation.

in two years; all were severe. The fourth patient had had two attacks of hematemesis, one of which occurred before splenic enlargement was noted. In the fifth patient the bleeding was

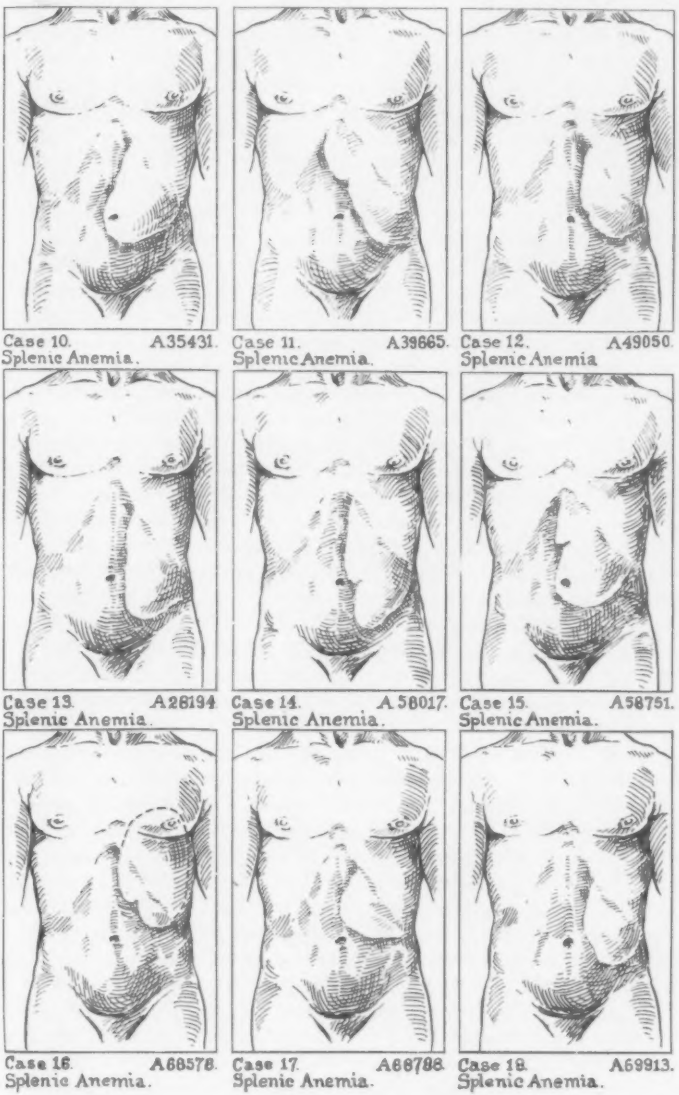

FIG. 2.—Contour and position of spleen as observed clinically before operation.

merely a regurgitation of blood. There was no instance of bleeding elsewhere than from the gastro-intestinal tract. One additional patient had spat blood probably from the throat at the time of menstruation for three years preceding operation. This has occurred much less frequently since operation.

The frequent occurrence of pain in the region of the spleen is a noteworthy incident in this series of cases. This symptom has not been generally discussed in connection with splenic anemia, and is probably caused by the perisplenitis which is so commonly present. Infarction may also be a cause of pain. In 12 of the 18 cases there was obtained a history of pain generally coming in prolonged periods at the left costal arch and often associated with tenderness. In 6 instances a history of acute attacks of pain was also obtained.

Fever was present in only two of these cases while under observation, and was not over 100°. However, cases regarded clinically as splenic anemia with fever have been reported. Two patients presenting conditions simulating splenic anemia who suffered from high fever, chills, and prostration in periodic attacks have been under our observation. These cases at first seemed to be atypical acute cases of splenic anemia. One of them at exploratory operation showed an advanced cirrhosis of the liver, and an omentopexy was done. The other is included in the second group of this series. Splenectomy was performed, but at operation evidences of gall-bladder disease were found, with many upper abdominal adhesions, and the spleen was not of enormous size. In this patient there were periodic and abrupt elevations of temperature to 105°, and at the same time the size of the spleen increased and upper abdominal pain of moderate severity was complained of. The condition of the spleen seemed to be secondary to a widespread abdominal infection, and not primary.

Diarrhea had been present in only 4 of the 18 cases. One of these was amebic and occurred in association with malaria ten years preceding operation. In another instance diarrhea had occurred in spells for one year, during which time splenic enlargement had been noted; the stool examination was negative. In the third case diarrhea had been troublesome for nine months, which was about five months preceding splenic enlargement. The fourth patient gave a history of diarrhea, which was mild and probably entirely incidental.

A history of malaria was obtained in only 4 cases. In 2 of these there may have existed some direct etiologic relationship. One patient had had malaria nearly every year up to the age of twenty-nine years, while splenic enlargement had been noted at times after the age of twenty-three years, which was twenty years before operation. Another patient, presenting a typical picture of the ascitic stage of Banti's disease, had had malaria eleven years preceding operation, at which time splenic enlargement had first been

noted. It is probable that chronic malaria produces a condition which eventually cannot be differentiated clinically from splenic anemia. The table of residences is as follows:

Alabama	1
Arkansas	1
Iowa	4
Michigan	1
Minnesota	3
Montana	1
New Mexico	1
New York	1
North Dakota	2
South Dakota	1
Virginia	1
Washington	1

A history of lues was not obtained in any of the cases grouped as splenic anemia. The Wassermann reaction was done on several of the more recent cases and was negative.

Cirrhosis of the liver was diagnosticated at operation in 5 of the 18 cases. In one additional patient clinical evidence of cirrhosis of the liver developed one year after operation, and the patient died later. In 2 other patients the liver was enlarged. In all, then, 8 of the 18 cases showed some change in the liver, while 5 were probably of the Banti type at the time of operation; 2 in the preascitic stage and 3 in the ascitic stage of Banti's disease. No case showed abdominal fluid without evidence of change in the liver at operation.

Jaundice was noted during the course of the disease twice, once with and once without evidences of cirrhosis. Melanoderma was noted in those cases seen by the writer, but no accurate information as to its occurrence in the series can be given.

The etiologic relationship of gall-bladder disease in connection with splenic enlargement may be of greater importance than is at present believed, both by reason of the possibility of infection and also through some influence upon the circulation in the closely related organs of the upper abdomen. Two cases of this series showed evidence of gall-bladder disease at operation, but the splenic enlargement was so great and the picture of splenic anemia so prominent that these cases have been retained in Group I. Moreover, 3 cases herewith reported in Group II showed gall-bladder disease, giving a total of 5 instances of gall-bladder disease in a group of 27 cases of splenomegaly (18.5 per cent.). This seems to be more than an accidental coincidence. One patient whose case was interesting in this connection had been operated on when fourteen years of age for gallstones. The gall-bladder was then removed; there were stones in the ducts and an enlarged spleen was found. Seven years later when splenectomy was done a diagnosis of Banti's disease was confirmed at operation. During the interim there had developed a progressive enlargement of the spleen with recurring attacks of anemia.

During the last two years while operating for other abdominal conditions a moderate enlargement of the spleen (three and four times normal) has been noted in 16 cases. In 8 instances it was associated with gall-bladder disease.

The operative mortality in the entire group of 27 cases was 2, or 7.4 per cent. One of these patients was in very poor condition and death occurred on the day of operation; moreover, this was an early case, the third of the series. In the 18 cases grouped as splenic anemia the postoperative results have been very satisfactory. Of the 16 patients who recovered from operation, 12 are in excellent health for periods varying from six months to seven years, 2 are improved, 1 improved for several months, but later developed ascites and died three years after operation, with symptoms of hepatic cirrhosis, and 1 died two and a half years after operation—the cause of death unknown. Of the 2 patients reported as improved, 1 shows normal blood, but is suffering from myocardial and renal insufficiency, while the other was operated upon six months ago; 4 of the 5 patients who showed evidence of cirrhosis of the liver at operation are in excellent health, 1 as long as seven years after operation. The results are shown in more detail by the following table:

GROUP I.—Postoperative Results. Cases Conforming Clinically to the Syndrome of Splenic Anemia.

Case.	No.	Year.	Time after operation.	Result.
1	(P3539)	1905	7 years	Well. Ascitic stage of Banti's disease. Spleen showed lymphocytic hyperplasia.
2	(G8869)	1907	1 day	Operative death. Ascitic stage of Banti's disease. Spleen showed endothelial hyperplasia.
3	(P7074)	1907	5½ years	Well. "Better health than ever." Spleen showed lymphocytic hyperplasia.
4	(A9315)	1908	4½ years	Well. Spleen showed endothelial hyperplasia.
5	(A10324)	1908	3 years	Improvement for several months. Death three years after operation. Ascites and dropsy (hepatic cirrhosis ?).
6	(A18026)	1908	4 years	Well.
7	(A20818)	1909	3½ years	General health excellent. Ascitic stage of Banti's disease.
8	(A22026)	1909	2½ years	Death, cause unknown.
9	(A27414)	1909	3½ years	Blood normal. Myocardial and renal insufficiency. No improvement in general health.
10	(A35431)	1910	5 days	Operative death.
11	(A39665)	1910	2½ years	Well. Symptoms probably due to arthritis deformans.
12	(A49050)	1911	1½ years	Well. No hemorrhages.
13	(A28194)	1911	1½ years	Excellent health. Preascitic stage of Banti's disease.
14	(A58017)	1911	1 year	Excellent health.
15	(A58751)	1911	1 year	Well. Spleen showed endothelial remains.
16	(A68578)	1912	6 months	Improved.
17	(A68788)	1912	6 months	Gained twenty-five pounds. Better health than for years. Preascitic stage of Banti's disease.
18	(A69913)	1912	4 months	Excellent health.

CONDENSED TABULATION—EIGHTEEN CASES OF SPLENECTOMY FOR SPLENIC ANEMIA.

Case.	Office No.	Name.	Date of Operation.	Sex.	Age.	Pathology.[2]	Postoperative condition.	Size of spleen.	Weight of spleen.	Duration of splenomegaly.	Pain in splenic region.	Size of liver.	Abdominal fluid.	Jaundice.	Hematemesis.	History of anemia.	History of malaria.	History of lues.	Old gall-bladder disease.
1	P3539	P. G. M.	Nov. 4, '05	F.	41	Lymphocytic hyperplasia	Sept. 24, '12. Well	To pelvis	3275G	4 yrs.	Neg.	+ (Cirrhosis)	+1	Neg.	Neg.	6 mo.	From 8 to 14 yrs. of age	Neg.	Neg.
2	G8869	B. S.	Jan. 7, '07	F.	27	Endothelial hyperplasia	Jan. 7, '07. Death day of operation	30x20x8 cm.	5280G	15 yrs.	2 yrs.	+ (Cirrhosis)	+3	+1	Neg.	10 yrs.	Neg.	Neg.	Neg.?
3	P7074	M. H. M.	May 17, '07	F.	27	Lymphocytic hyperplasia	Sept. 27, '12. Well	To pelvis	2190G	1 yr. +	1 yr.	Normal	Neg.	Neg.	Neg.	1 yr.	Neg.	Neg.	Neg.?
4	A9315	B. L. T.	May 11, '08	F.	37	Some areas of endothelial hyperplasia	Sept. 25, '12. Well	30x20x7½cm.	895G	9 mo. +	9 mo.	Normal	Neg.	Neg.	Neg.	?	Neg.	Neg.	Neg.?
5	A10324	A. V. L.	July 2, '08	F.	49	Chronic splenitis	Improved for several months. Death, May 19, '11	21 cm.	1450G	9 mo. +	Neg.	Normal	Neg.	Neg.	Neg.	9 mo.	Neg.	Neg.	Neg.?
6	A18026	H. N.	Dec. 31, '08	M.	26	Chronic splenitis	July 10, '12. Well	18 cm.	425G	2 yrs. +	2 yrs.	Normal	Neg.	Neg.	Neg.	5 mos.	Neg.	Neg.	Neg.?
7	A20818	C. K.	Mar. 4, '09	M.	30	Chronic splenitis	Sept. 25, '12. Well	20 cm.	1180G	10 yrs.	4 yrs.	Reduced (cirrhosis)	Neg.?	Neg.	4 times severe	2 yrs.	11 yrs. before	Neg.	Neg.
8	A22026	J. D. B.	Apr. 14, '09	F.	53	Chronic splenitis	Dec. 15, '11. Death. Cause unknown	20 cm.	1670G	3½mo. (8 yrs.?)	8 yrs.	Normal	Neg.	Neg.	Regurgitation	4 mos.	Neg.	Neg.	Neg.
9	A27414	C. M. H.	Aug. 11, '09	M.	45	Chronic splenitis	Sept., '12. Hb. 90 per cent. Cardiac and renal symptoms	32x25 cm.	1514G	4 yrs.	4 yrs.	Normal	Neg.	Neg.	Neg.	2 mos.	Neg.	Neg.	Neg.
10	A35431	W. J. P.	May 3, '10	M.	39	Chronic splenitis	May 9, '10. Death on fifth day	25x20 cm.	575G	15 yrs.?	2 mos.	Normal	Neg.	Neg.	Once a yr for 15 yrs.	15 yrs.	Neg.	Neg.	+ Stones?
11	A39365	T. O. B.	July 4, '10	F.	50	Chronic splenitis	Oct. 19, '12. Well. Arthritis deformans	30 cm.	1385G	4 mo. + (9 mo.?)	3 mos.	Normal	Neg.	Neg.	Neg.	6 mos.	Neg.	Neg.	Neg.
12	A49050	F. F.	Feb. 27, '11	M.	23	Chronic splenitis	Aug. 22, '11. Well	24x20 cm.	879G	2 yrs.	Neg.	Normal	Neg.	Neg.	4 times	2 yrs.	Neg.	Neg.	+ Stones
13	A28194	R. K.	June 30, '11	F.	22	Chronic splenitis	June 29, '12. Well	25x18x8 cm.	1530G	7 yrs.	Neg.	+1 (Cirrhosis)	Neg.	+1	Neg.	7 yrs.	Neg.	Neg.	Neg.
14	A58017	E. J. J.	Sept. 7, '11	F.	43	Chronic splenitis	Sept. 23, '12. Well	20x12x8 cm.	610G	20 yrs.	5 yrs. +	Normal	Neg.	Neg.	Neg.	5 yrs. +	Up to age of 29	Neg.	Neg.
15	A58751	C. W.	Sept. 26, '11	F.	25	Some areas of endothelial remains	Sept. 22, '12. Well	32x20x12 cm.	4500G	8 yrs.	6 wks.	Normal	Neg.	Neg.	Spat blood with menses	Neg.	Neg.	Neg.	Neg.
16	A68578	A. C.	June 5, '12	F.	56	Chronic splenitis	July 16, '12. Improved	18x12x8 cm.	980G	6 mo. +	Neg.	Normal	Neg.	Neg.	Neg.	6 mos.	Neg.	Neg.	Neg.
17	A68788	A. J. S.	June 18, '12	F.	37	Chronic splenitis	Nov. 12, '12. Well	20x12x9 cm.	890G	9 mos. (4 yrs.?)	Neg.	+2 (Cirrhosis)	Neg.	Neg.	Twice	9 mos.	Neg.	Neg.	Neg.
18	A69913	S. H.	July 5, '12	M.	49	Chronic splenitis	Aug. 24, '12. Well	19x11x9 cm.	1000G	2 yrs. (3 yrs.?)	2 yrs.	+2 (No cirrhosis)	Neg.	+at onset	Neg.	6 mos.	As a boy	Neg.	Neg.

[2] For a discussion of the pathology see "The Pathology of Splenomegaly: A Study of the Operative and Autopsy Material from the Mayo Clinic (St. Mary's Hospital)," by L. B. Wilson. Surgery, Gynecology, and Obstetrics, vol. xvi, 1913.

BLOOD FINDINGS IN EIGHTEEN CASES OF SPLENECTOMY FOR SPLENIC ANEMIA.

Case No.	Time of count.	Hemoglobin.	Erythrocytes.	Leukocytes.	Small lymphocytes	Large lymphocytes.	Polymorphonuclears.	Myelocytes.	Eosinophiles.	Basophiles.	Transitionals.	Normoblasts.	Megaloblasts.	Poikilocytosis.	Polychromatophilia.
		%			%	%	%		%	%	%				
1 (P3539)	2 days before operation.	50	4,504,000	1,600											
	7 years after operation.	70	3,800,000	8,600											
2 (G8869)	2 days before operation.	80	5,200,000	4,800											
3 (P7074)	1 day before operation.	57	5,080,000	2,000											
	5 yrs. 8 mos. after operation.	85	4,800,000	3,000											
4 (A9315)	2 weeks before operation.	40	..	4,600											
	7 months after operation.	70	4,280,000	2,700											
	3 weeks before operation.	50	2,960,000	5,600	..	..	..	..	..	..	..	Smears negative			
5 (A10324)	1 week before operation.	70	..	9,500	..	..	..	..	..	..	..	Smears negative			
	3 weeks after operation.	..	..	34,800	4.0	..	93.0	..	3.0						
6 (A18026)	3 days before operation.	82	..	7,000	22.5	..	70.0	..	2.0	0.5					
	6 months before operation.	20	1,200,000												
	2 days before operation.	47	3,300,000	2,500	17.5	7.0	73.0	..	1.5	0.5	0.5				
7 (A20818)	10 days after operation.	55	..	9,900	5.6	5.0	86.6	..	0.6	..	2.3	..	+		
	3 weeks after operation.	45	3,740,000	12,400	6.0	8.0	85.5	..	..	0.5					
	4 months after operation.	80	4,000,000	8,700											
	3½ years after operation.	90+	5,000,000	8,500											
	2 weeks before operation.	68	3,600,000	2,500	23.0	3.0	72.0	..	..	1.0	1.0				
8 (A22026)	2 weeks after operation.	60	4,640,000	7,700											
	4 weeks after operation.	68	5,160,000	7,800	19.6	10.4	64.4	..	4.0	0.8	0.8				
	3 days before operation.	75	4,360,000	11,000	12.3	1.3	80.6	..	3.3	2.0	0.3	..	2	+	+
9 (A27414)	1 month after operation.	50	3,090,000	28,800	13.0	8.6	72.3	..	3.0	2.3	0.6				
	3 years after operation.	95	5,600,000	10,500	?	2.5	79.0	4	7.5	..	..	..	..	+	
10 (A35431)	2 months before operation.	35	3,030,000	3,200	13.6	5.0	78.6	..	1.0	1.0	0.6	1	..	+	
	1 week before operation.	69	4,600,000	3,400	..	..	..	..	..	..	..	Smears negative		+	
11 (A39665)	12 days before operation.	50	4,550,000	1,000	43.0	19.0	30.0	1	..	2.0	5.0	..	..	+	
	18 days after operation.	75	4,330,000	3,350	35.5	21.0	37.5	..	4.0	1.0	1.0	..	..	+	
	2 years after operation.	90	4,000,000	5,144											
	6 days before operation.	65	5,420,000	3,750	16.5	8.5	73.5	..	1.0	..	0.5	..	..	+	
12 (A49050)	2 weeks after operation.	67	5,680,000	14,200	16.3	6.0	73.3	..	1.0	2.3	1.0	..	..	+	
	2½ years after operation.	80	4,960,000	11,750											
	2 weeks before operation.	60	2,950,000	7,900	22.0	2.0	74.0	..	1.0	1.0					
13 (A28194)	2 weeks after operation.	85	4,800,000	9,200	15.0	4.5	76.0	..	3.0	1.5	..	..	..	+	
	1 year after operation.	90													
14 (A58017)	5 days before operation.	90	4,900,000	3,400	21.5	6.5	68.5	..	0.5	1.0	2.0				
	3 weeks after operation.	89	4,820,000	7,200	26.5	8.0	64.0	..	0.5	..	1.0				
	2 weeks before operation.	70	3,970,000	4,900	26.7	8.0	60.7	..	4.3	..	0.3	1	..	+	
15 (A58751)	2½ weeks after operation.	75	4,760,000	12,500	19.7	6.0	71.0	..	2.7	0.7					
	1 year after operation.	100	4,800,000	15,000	Differential count not abnormal										
16 (A68578)	2 days before operation.	50	4,200,000	5,100	13.0	2.0	78.0	..	3.3	2.7	1.0	..	..	+	
	4 weeks after operation.	60	4,320,000	15,600	11.0	9.0	77.7	..	1.7	0.3	0.3	1	..	+	
	3 days before operation.	55	4,600,000	2,700	19.4	8.0	70.0	..	2.0	..	0.6	..	..	++	+
17 (A68788)	2 weeks after operation.	70	..	14,200											
	5 months after operation.	88	4,800,000	10,800	46.7	2.3	45.3	..	1.3	2.0	2.3				
18 (A69913)	1 week before operation.	45	5,080,000	5,500	30.0	9.7	57.0	..	1.7	0.7	0.7	..	..	+	
	3 months after operation.	90													

NOTE.—A differential count of 200 or 300 cells was made in these cases. All cases save numbers 4 and 15 gave histories suggesting the intermittent recurrence of anemia. Where many counts were made a representative selection is given.

GROUP II. Infectious (?) splenomegaly (4 cases). Four cases of this series could not well be classified as splenic anemia. The histories were more or less complicated by the occurrence of other affections, suggesting that splenomegaly was not primary. It will be noted that 3 of the 4 patients eventually died, though there were no operative deaths. The division of these cases, as will be inferred from the histories, was made without any reference to the postoperative course. It is not my purpose to discuss these cases in detail, but rather to give their salient features in order that the evidence for excluding them from Group I may be clear. In many respects this small group of cases is the most interesting of the series.

CASE I (A34196).—J. E. G., male, aged fifty-five years. The chief complaint in this instance was of recurring attacks of upper abdominal pain of moderate severity. There was no history suggestive of ulcer and a clinical diagnosis of cholecystitis with splenomegaly was made. The enlargement of the spleen had not been noted before examination. There was nothing in the history which was suggestive of splenic anemia. At operation adhesions were found around the appendix, gall-bladder, and pylorus. The duodenum was bound to the pancreas and an ulcer may have been present. The spleen weighed only 320 grams and showed no connective-tissue hyperplasia. Splenectomy was the only operation performed, and the patient is in excellent health one and one-half years afterward.

CASE II (A59392).—W. P. D., female, aged thirty-seven years. For two years associated with three successive pregnancies there were similar attacks of illness, apparently without definite evidence of pelvic inflammatory disease. These attacks were characterized by the recurrence of severe chills and high fever, even to 105° and 106°, and upper abdominal pain of an indefinite nature. The last attack was the most severe and prolonged. During these attacks the spleen became very much enlarged. Examination and special tests were negative for malaria, syphilis, and tuberculosis. Blood cultures and examination of the blood for Leischmann-Donovan bodies were also negative. The patient's general condition was very poor as a result of her protracted illness. Hemoglobin, 70 per cent.; red blood cells, 4,060,000; white blood cells, 3100. Differential count was not abnormal. At operation evidence of widespread infection was found. There were adhesions in the pelvis, but particularly about the gall-bladder and common duct, was there evidence of old disease. The vessels of the spleen were brittle. The weight of the spleen was 640 grams, and pathologically the organ showed considerable increase in connective tissue. After operation the liver, which had been enlarged, became reduced to normal, and the symptoms abated somewhat. The patient gradually lost weight and strength, however, and died

NOTE.—A differential count of 200 or 300 cells was made in these cases. All cases save numbers 4 and 15 gave histories suggesting the intermittent recurrence of anemia. Where many counts were made a representative selection is given.

four and a half months later with nephritis which may have been entirely a terminal condition. Anemia never became extreme. An autopsy was not obtained. In this instance the splenomegaly was doubtless part of a peculiar chronic infectious process.

CASE III (A65749).—J. G., male, aged thirty-three years. This patient presented a rather complex history. What was probably a luetic sore had been present fourteen years before operation; the Wassermann reaction, however, was negative at the time of examination. Nine years and five months before operation hematemesis had occurred. The appearance of blood in the stool had been noted oftener than hematemesis, four times in the last three years. Splenomegaly had been present three years. The blood count was: Hemoglobin, 92 per cent.; red blood cells, 5,480,000; white blood cells, 7600. Differential not abnormal. The spleen extended to the level of the navel. Pathologically the spleen showed connective-tissue increase and infarcts. Its size was 21 x 15 x 7 cm. and its weight 900 grams. Death occurred two months after operation. At autopsy an acute nephritis, with cardiac dilatation, was found. In addition, tuberculous mediastinal and retroperitoneal lymphatic glands and a duodenal ulcer were discovered. Although the history in some respects suggested splenic anemia, in this case the pathologic findings prevent us from so classifying it. Hematemesis, which occurred before operation, may or may not have been due to bleeding ulcer.

CASE IV (A14838).—B. F. S., female, aged fifty-seven years. Raynaud's disease had been first diagnosticated five years before operation in this case and thyroidectomy for exophthalmic goitre had been performed four years previously. Rheumatoid arthritis had been present for three years. The spleen had been enlarged for three years, with rapid growth for six months, and at the time of operation it extended to the level of the anterior superior spine of the ileum. The blood count was: Hemoglobin, 84 per cent.; red blood cells, 5,600,000; white blood cells, 21,800. The differential count showed a polymorphonuclear leukocytosis of 93 per cent. At operation the spleen was found to measure 20 x 15 x 10 cm. and weighed 1340 grams. The patient also had gallstones, which it was thought should be removed later, and the liver was somewhat enlarged. A small piece of pancreas was ligated and cut away with the spleen. The patient died six weeks later, and at autopsy chronic nephritis and chronic general peritonitis were found.

GROUP III. The remaining cases are grouped together for convenience: Wandering spleen, tuberculosis, cirrhosis of the liver, and pernicious anemia are considered.

(*a*) *Two Cases of Wandering Spleen.* Wandering spleen is, as a rule, readily diagnosticated if only the possibility of its occurrence be kept in mind. It has often been mistaken for movable

kidney. It has remained unrecognized when simple methods of exclusion and careful palpation would have decided the diagnosis definitely. One of these patients (A11038) was neurotic, but com-

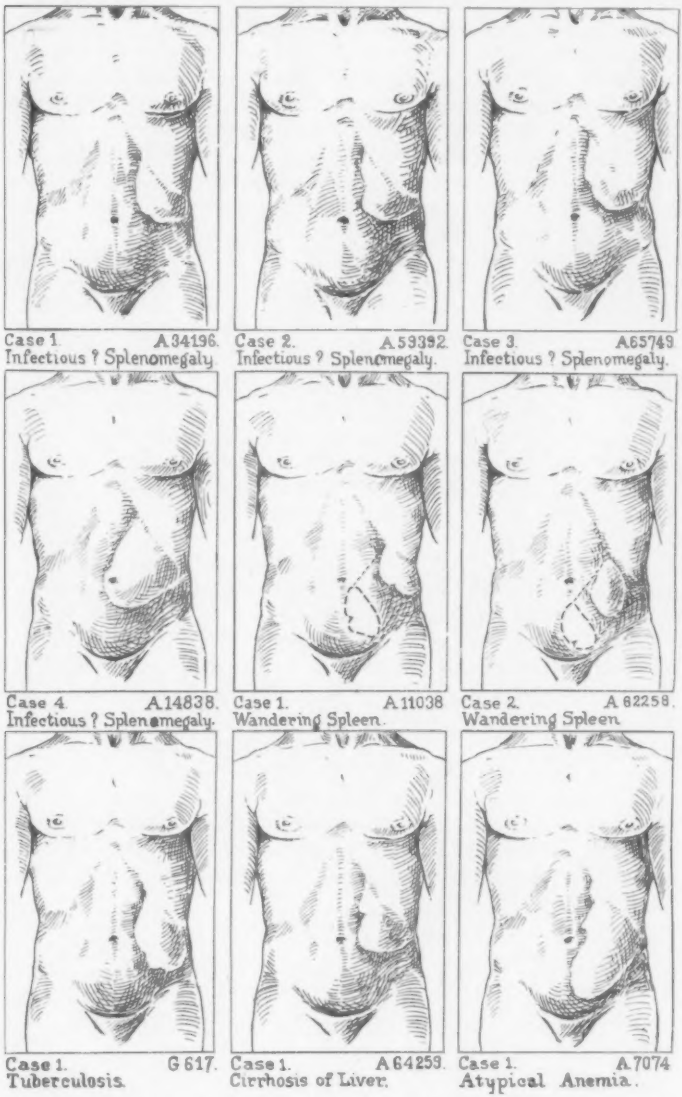

FIG. 3.—Contour and position of spleen as observed clinically before operation.

plained of pain over the spleen to a degree which seemed to warrant splenectomy. A moderate grade of anemia was present. Four years after operation the patient's blood count is normal, though she complains of many neurotic symptoms. The second patient (A62258) had complained of recurring attacks of pain of an hour's duration for a period of four years. At operation a twisted pedicle was found, while the spleen could be moved to the lower abdomen and to the right of the median line, though it lay naturally opposite the navel. This patient is well.

(*b*) *One Case of Tuberculosis of the Spleen* (G617). Multiple abscesses and tuberculous deposits studded the organ, giving the appearance so commonly seen in the kidney. The length of the history had been sixteen months, and no definite evidence of tuberculosis was found elsewhere in the body before operation. The patient died four months later, however, with evidences of a disseminated tuberculosis. An autopsy was not obtained.

(*c*) *One Instance where Cirrhosis of the Liver Seemed to be Primary* (A64259). Although the patient was only twenty years of age, all parts of the liver were covered with contracted areas, while in volume the organ was increased. It was the opinion of the surgeon (W. J. Mayo) that the cirrhosis was primary. The weight of the spleen was 750 grams, and there was nothing in the pathology which indicated lues. This patient gave a history of splenomegaly for one year and recurrent anemia for two years. The blood count showed a secondary type of anemia, with a hemoglobin of 58 per cent. The leukocyte count was 4200. The patient developed ascites, and died two months after operation. An autopsy was not obtained.

(*d*) *One Case of Pernicious Anemia* (?) (A7074). In this instance the hemoglobin was low (45 per cent.), the color index was high, but less than one, and a few normoblasts and megaloblasts were found in the smears. After operation, however, a shower of normoblasts and megaloblasts occurred. The spleen extended below the navel and weighed 1640 grams. The patient, two and a half years after operation, states that he is weak and anemic, and unable to work, and a review of the case suggests the diagnosis of an atypical pernicious anemia. It has been impossible, however, to obtain a recent blood count, and the diagnosis at best remains very uncertain.

STATISTICAL SUMMARY.

Total number of splenectomies	27
Operative deaths	2 (7.4 per cent.)

Group I. Splenic anemia.	Cases.
Well from six months to seven years (longer than one year, 10)	12
Improved (1, blood normal, myocardial and renal insufficiency; 1 operated on six months ago)	2
Improvement several months, death three years after operation (hepatic cirrhosis?)	1
Death two and one-half years after operation, cause unknown	1
Operative deaths	2—18

Banti's syndrome (included above).	
Operative death	1
Well (seven years, three and one-half years, one and one-half years, six months)	4—5
Spleens showing chiefly connective-tissue hyperplasia	13
Spleens showing lymphocytic hyperplasia	2
Spleens showing endothelial hyperplasia (Weichselbaum or Gaucher type)	3
Group II.	
Infectious (?) secondary splenomegaly.	
Well	1
Died from two to six months	3—4
Group III. Miscellaneous.	
Wandering spleens, well	2
Tuberculosis, death in four months	1
Atypical anemia (?), unimproved two and one-half years	1
Cirrhosis of liver, death in two months (ascites)	1—5

A consideration of this series of cases, in which splenectomy was done, impresses one with the fact that a proper grouping of conditions, in which marked enlargement of the spleen is associated, with an anemia of the secondary type is extremely difficult if not impossible at the present time. The clinical features form the best basis for a tentative classification, and especially assist us in recognizing clear-cut and uncomplicated cases of splenic anemia. The pathology of splenic anemia and those conditions which simulate it is too little understood, and conclusions for the present would best be drawn only from those reported cases in which pathological as well as clinical evidence has been published.

This review may also have indicated a possible relationship between gall-bladder disease and splenomegaly. It seems to have indicated more clearly, however, that there is a clinical syndrome conforming to the general conception of splenic anemia in which splenectomy is followed by a return to excellent health in a large percentage of cases, but in those instances in which the diagnosis is complicated by other diseases of a chronic infectious nature, the value of splenectomy is questionable.

It is necessary in these as it is in other medicosurgical conditions for the physician to learn the details of surgical prognosis. Splenectomy should be advised only after careful diagnosis, not only of the abdominal enlargement itself but also of the patient's general condition, and after the elimination of the existence of serious complications.

NOTE.—The reader is referred to the following articles: "Principles Underlying Surgery of the Spleen, with a Report of Ten Splenectomies," by W. J. Mayo, *Jour. Amer. Med. Assoc.*, January 1, 1910; "Surgery of the Spleen," by W. J. Mayo, *Surg., Gyn., and Obst.*, xvi, 1913; "The Pathology of Splenomegaly: A Study of the Operative and Autopsy Material from the Mayo Clinic (St. Mary's Hospital)," by L. B. Wilson, *Surg., Gyn., and Obst.*, xvi, 1913.

The author is indebted to H. G. Wood and A. Archibald for their assistance in compiling statistical data of the cases reported.

THE ADMINISTRATION OF OX BILE IN THE TREATMENT OF HYPERACIDITY AND OF GASTRIC AND DUODENAL ULCER.

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The value of internal therapeutic measures is so difficult of conclusive proof that the following suggestion is offered with some hesitation. Yet in view of the strength of the physiological and pharmacological facts upon which the theoretical considerations have been based, and from the practical results obtained in some fifty preliminary cases, it is felt that the matter deserves publication in the hope that its worth may be tested by other physicians.

Our knowledge of the physiology of the stomach, particularly in regard to the functions of the pylorus, has in recent years made great advances. Clinicians, however, have been slow to attempt to utilize the new knowledge of normal physiology to shed light upon the pathological physiology of clinical disorders. This may be due in part to the widespread spirit of pessimism with which the subject of the medical diseases of the stomach is so commonly regarded; for this chapter in the recent history of internal medicine has not been a bright one. Our power to furnish relief in cases complaining of dyspepsia has remained far from satisfactory. For the purpose of determining treatment that can be recommended with confidence that improvement will result, the study of the stomach contents has not justified the hopes that were formerly held. In the diagnosis of pyloric stenosis, it is true, the examination of the gastric contents is of great importance, and some assistance is obtained in questions of carcinoma; but in the diagnosis of the functional diseases, and even of gastric and of duodenal ulcer, the aid obtained by means of test meals is so slight as hardly to justify the trouble to the examiner and the discomfort to the patient. For purposes of classification of cases investigation of gastric contents has led to the recognition of certain abnormalities of function, such as hyperacidity, hypersecretion, etc.; but even in these no complete explanation of the symptoms has been reached. and over them but little therapeutic control has been gained. A complete reconsideration of the subject without bias from previous clinical teachings is therefore desirable.

In common clinical experience the most frequent form of dyspepsia is that characterized by "sour stomach" and "heart-burn," or pain after eating. Cases of this are seen almost daily in every large clinic. They are commonly regarded as cases of hyperacidity, but while many of them do show hyperacidity in the test breakfast

withdrawn after an hour in many others the contents are not abnormal. The surgical findings of late years have shown that many of the more severe of these cases have gastric or duodenal ulcers, but it is still too advanced a view to maintain that ulcer is present in all. Thus in routine practice an uncertain diagnosis is made of hyperacidity or ulcer. In treatment the patient is given directions and diet according to the physician's opinions, and an alkali to be taken for palliation as necessary; but in many cases no appreciable improvement results.

This state of affairs is not an inspiring one, yet we must face the fact that with the best intentions in the world and with many new resources at our command it has been hardly possible to advance our power to benefit these cases beyond that of the physicians of past generations, unless we yield to the demands of the surgeons and consent to exploratory laparotomies by wholesale. Present methods of clinical examination have failed us beyond a certain limited extent, and have left us still to wait for new developments. But rather than wait passively for new power to come to us it is our duty to search constantly for ways around the difficulties which we cannot surmount, and to follow any new paths still unexplored, however slight their promise may seem.

Instead of sifting objective evidence let us consider for a moment in detail the subjective sensations as described by the more intelligent patient through a sample day. He rises and goes to breakfast without symptoms. He eats his breakfast and other meals with relish, but with well-justified apprehension; he leaves the table still without discomfort, but within a short time he becomes conscious of a burning sensation, as from a chemical irritant clearly referred to the same point to which hot fluids ingested by the mouth can be traced, unquestionably to the stomach. The discomfort gradually increases; belching and acid regurgitation may occur. Then after an hour or more of suffering the symptoms gradually pass off, only to recur after the next meal.

Now in all this process there is one point which is to be noted above all others. This is that through it all the patient's one longing is that the stomach may become emptied of its contents as soon as possible. Many patients are conscious that vomiting will give relief, and induce it for that purpose; but more, while no less conscious that evacuation of the stomach is to be wished for, simply endure the distress as best they can until the meal has passed through the pylorus. The association in the mind of the intelligent dyspeptic between an empty stomach and relief is an invariable one. Can we not therefore take the hint and consider whether the cause of symptoms may not be a disorder of the normal function by which the stomach discharges its acid contents into the duodenum through the pylorus?

Let us therefore review the physiology of the pylorus to see if there

is any way in which its action may with any likelihood be disturbed so as to interfere with the prompt passage of gastric contents of normal or increased acidity through its opening. According to Cannon[1] the control of the pyloric sphincter depends upon two factors. The signal for the first opening is the appearance of free acidity on its gastric side. This allows a jet of acid chyme to enter the duodenum. The presence of acid in the duodenum, however, is a signal for the closure of the pylorus, which continues to act until this acid in the duodenum is neutralized, after which if the contents before the pylorus are still acid the sphincter may relax again and repeat the process. But so long as the contents of the duodenum are acid the pylorus cannot open, no matter how high may be the acidity on its gastric side. For the proper functioning of the pylorus, therefore, it is necessary to have a proper balance between acid secretion on the part of the stomach and acid-neutralizing power in the duodenum. While the periodic opening of the pylorus will be delayed if gastric acidity is deficient, it will also be delayed if the neutralizing fluids in the duodenum are deficient. Now we know that in the cases which we have been considering the gastric acidity is at least normal and is often increased. May it not be that it is the neutralizing power of the fluids in the duodenum that is at fault, unduly prolonging the period during which the acid secretion of the stomach accumulates before the pylorus awaiting its discharge?

The neutralization in the duodenum of acid contents received from the stomach is effected by the bile and by the pancreatic juice, as well as by secretion of the duodenal mucosa described by Pilcher.[2] While the amount of the second and the third of these cannot be influenced, the flow of bile, as shown by Pfaaf and Balch,[3] can easily be increased by the administration by mouth of ox bile. Thus since the possibility that so-called hyperacidity and even gastric duodenal ulcer may owe their symptoms to delayed neutralization of duodenal contents is not beyond the range of the imagination, and since if present such delayed neutralization should theoretically be corrected by the administration of ox bile, a series of cases with symptoms of these conditions has been treated in this way as a therapeutic experiment.

The clinical test thus undertaken comprises somewhat over fifty cases, which can be regarded as typical of the class formerly considered as hyperacidity, but now after the teachings of Moynihan and Mayo under the suspicion of chronic gastric and duodenal ulcer. The clinical histories are not individually of such interest that detailed description is desirable. Their most prominent symptoms were pain and pyrosis following the ingestion of food

[1] The Mechanical Factors of Digestion, 1911.
[2] Amer. Jour. Med. Sci., 1911, cxlii, 687.
[3] Jour. Exper. Med., ii, 49.

after a more or less definite interval and relieved temporarily by sodium bicarbonate. Vomiting occurred occasionally in a minority of the cases, and when it occurred invariably gave relief, so that some frequently induced vomiting to stop the pain. In four cases there was a clear history of more or less recent hematemesis. In one case an *x*-ray examination showed the appearance of an extensive gastric ulcer. In two cases ulcer had been demonstrated at operations. The great majority were office and out-patient cases, whose daily habits continued unchanged during observation.

The treatment was as follows: A general diet list was given merely to avoid clearly unsuitable foods; this was regarded by the experienced patients as a generous one. A caution against overeating was given, and stress was laid upon thorough mastication to insure prompt action upon the food by the gastric juice. The ox bile was given in pills prepared by a Boston pharmacist according to the directions of Pfaff,[4] each containing 0.25 gram of dried and pulverized ox bile, salol coated to conceal the taste and to prevent dissolution in the stomach. Two or three of these pills were given after meals three times a day for a week, after which, as a rule, the number was reduced. In some instances where the appetite was not good, or where there was other reason to suspect that the gastric secretion was not always active, dilute hydrochloric acid and tincture of nux vomica, of each eight minims, were given in water before meals, and for temporary relief sodium bicarbonate and milk of magnesia were recommended to the few patients not already familiar with them. Aside from these measures, and laxatives when needed for constipation, the daily life of the ambulatory patients continued as before, and in the less numerous cases in bed on account of hematemesis or other severe symptoms as little other treatment was given as possible.

The results of this treatment were such as to lead the author to the belief that they could not be explained by the general directions given, but must be laid to the influence of the bile. In practically all cases followed the patients described a satisfactory improvement beginning within a few days, and at the end of a week or ten days gave a highly favorable report of their condition. The seven cases in which from hematemesis or other special evidence the presence of ulcer was undoubted are too few, it is true, from which to draw final conclusions; yet with one possible partial exception their course was no less favorable than that of the less serious cases. The four with a history of vomiting blood all promptly became free from symptoms, although two of them refused to give up their work, and were therefore treated as ambulatory cases. The patient whose *x*-ray plates gave the appearance of ulcer became free from pyrosis and pain, although some feelings of distress,

[4] Loc. cit.

possibly neurotic, persisted. Of the cases with ulcers demonstrated at operation the following brief descriptions may be given: The first was a woman in whom during an operation for fibroid a pyloric ulcer was found. She had for many years had daily attacks of pain after eating so severe that she frequently induced vomiting for their relief. Under the ox bile treatment she rapidly improved, but in spite of this a gastro-enterostomy previously determined upon by the surgeon was performed. The other case had had a gastro-enterostomy performed for a demonstrated duodenal ulcer in 1908. In 1910, at a second operation, a deep ulcer was found in the jejunum opposite the stoma, which was resected with obliteration of the gastro-enterostomy. Hardly had he recovered from this second operation when symptoms returned. The bile treatment was then instituted and he became free from symptoms for a year. At the end of that time, however, he reported that the pains had recurred and that he had taken the pills which he still had without relief. A prescription for some fresh pills was given him, and he did not return. On account of a change of residence he could not be traced, so that the outcome is uncertain.

But it is not the purpose of this paper to advocate the use of ox bile as the sole treatment of gastric and duodenal ulcer. It is in cases of dyspepsia of a milder type in which even bed treatment is not considered necessary that the treatment is most clearly supported by its results. In no typical instance among the cases followed has pyrosis and pain directly connected with eating failed to be relieved; in two apparent exceptions it turned out that the patients had not had the prescription filled. In one somewhat atypical patient, to whom, however, the treatment was given, no benefit was obtained; he later showed marked improvement and gain in weight under antisyphilitic treatment. Still later he drifted into the hands of a surgeon who explored him, but was unable to find any organic lesion. Cases in neurotic persons were somewhat less constantly entirely relieved, but many extremely neurotic patients were enthusiastic over the benefit received. In a word, from the experience of the past two years dyspeptics of the so-called hyperacidity type, which were formerly treated with very indifferent success, have when treated in the same way but with in addition the use of salol-coated ox-bile pills seemed to obtain relief. It is therefore hoped that in the hands of others the treatment may prove no less successful.

SUMMARY. There is reason to suspect that in hyperacidity and in gastric and duodenal ulcer the symptoms are at least in part due to delay in the neutralization of the acid contents discharged into the duodenum. The administration of ox-bile pills (salol coated) by the mouth should theoretically correct this fault. Empirically such administration of ox-bile has seemed to be of service in the relief of pyrosis and pain after eating; it has been followed by improvement in cases of gastric and of duodenal ulcer.

In conclusion, it must be stated that if the method here described proves of value the chief credit is due to the teachings of Cannon and of Pfaff, of which it is but a practical application.

NOTE.—While the proof-sheets of this article were in hand a third patient, omitted by oversight from this group, called for advice in an acute respiratory infection. In February, 1911, at operation for gallstones, a duodenal ulcer was found, and on his leaving the hospital the ox-bile treatment was given. Since then he has not had to consider his digestion except to take an occasional dose of sodium bicarbonate after indiscretions in diet.

OBSERVATIONS ON THE INTESTINAL BACTERIA IN PELLAGRA.[1]

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(From the Laboratories of the New York Post-Graduate Medical School and Hospital.)

A GENERAL survey of the fecal bacteria in pellagra was undertaken in 1910 and 1911 by the Illinois State Pellagra Commission. A brief summary of that work has been published[2] and the detailed record of the work has also recently appeared.[3] In general it was ascertained that the fecal bacteria in pellagra, when examined directly with the microscope, are different from the normal in their quantitative relationships, and that unusual kinds of bacteria, more or less heterogeneous in nature, are present. The cultural tests also brought to development unusual quantities of certain normal types, Bacillus bifidus, Bacillus welchii, and micrococci, in some cases, as well as a considerable variety of bacterial forms not ordinarily found in the feces of healthy men. None of these changes appeared to be constant. During the acute attack accompanied by diarrhea the Gram-positive cocci were nearly always abnormally numerous, and the Gram-negative bacilli were less numerous than normal in these cases. These changes were also observed in the subacute cases and even persisted to a slight degree after recovery from the skin lesions. The percentage of these cocci and bacilli are indicated in Chart I, along with data of similar observations on healthy men[4] for comparison. These changes,

[1] This paper forms a part of the progress report of the Thompson-McFadden Pellagra Commission of the New York Post-Graduate Medical School.

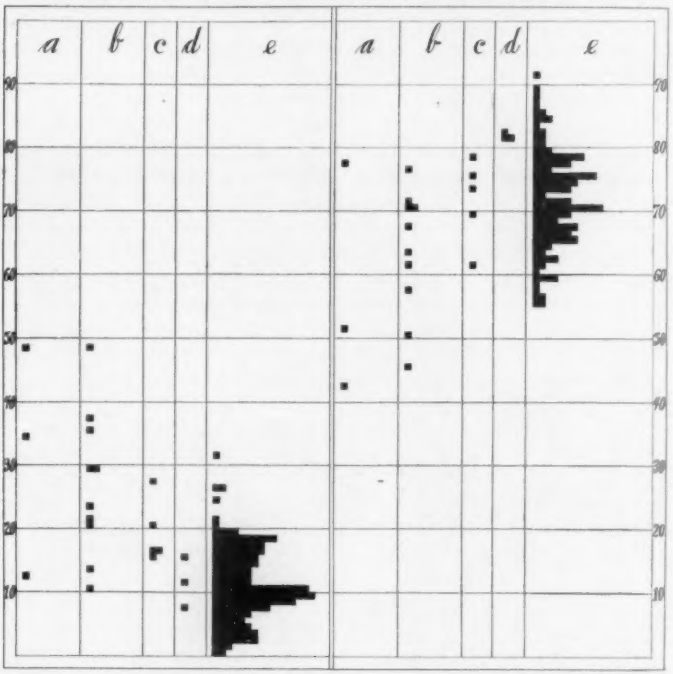
[2] Pellagra in Illinois, Arch. Int. Med., August and September, 1912, x, 123 to 168, 219 to 249.

[3] Report of the Pellagra Commission of the State of Illinois, Springfield, Illinois, 1912.

[4] Jour. Infect. Dis., April, 1909, vi, 123 to 169.

which were nearly constant, were such as might be expected as a natural result of the digestive derangement. There was no indication of a substitution of the normal intestinal bacteria by an abnormal invader. The abnormal types were various in nature and in no case dominant in numbers.

CHART I.—Percentage of gram-positive cocci and of Gram-negative bacilli in the feces.



Percentage of Gram-positive micrococci and of Gram-negative bacilli in the feces: (*a*) three examinations in acute pellagra; (*b*) ten examinations in subacute pellagra; (*c*) four examinations after recent recovery from pellagra; (*d*) three examinations in insane individuals not pellagrins; (*e*) one hundred and thirty-seven examinations in healthy men. The data for *a*, *b*, *c*, and *d* are taken from MacNeal, Allison, and York, Report of the Pellagra Commission of the State of Illinois, Springfield, 1912, pp. 55 to 160, and the data for *e* from MacNeal, Latzer, and Kerr, the Fecal Bacteria of Healthy Men, Jour. Infect. Dis., 1909, vi, 123 to 169.

During the course of the primary examinations subcultures were made from a number of colonies and preserved for subsequent study. One hundred of these bacterial strains were subjected to agglutination tests, using the blood serum from cases of pellagra and from normal individuals. Three of the one hundred strains reacted in a somewhat suggestive manner. These were strains Nos. 14, 35, and 67. All were derived from cases of pellagra at

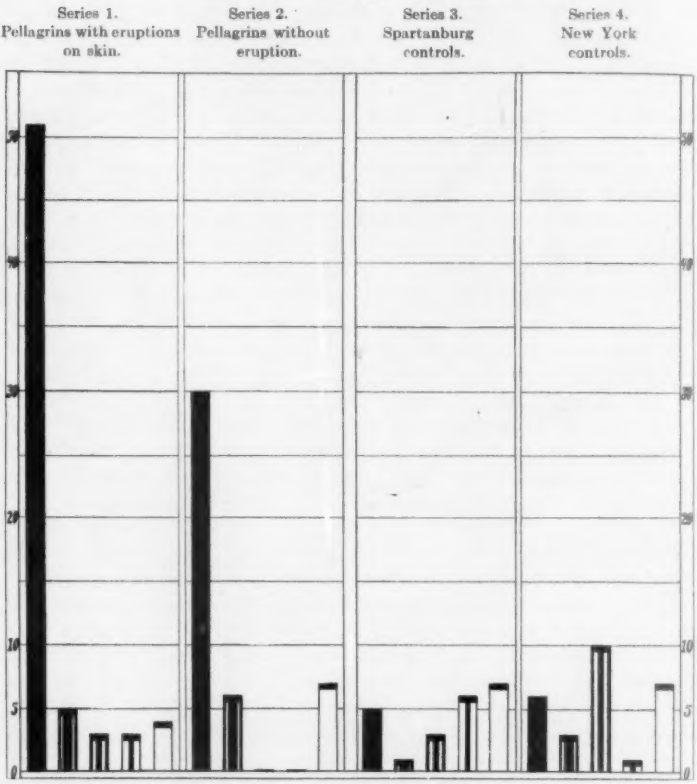
Peoria, Illinois. They were agglutinated by sera of pellagrins at Peoria, at Kankakee, and at Chicago. The suggestion of a specific relationship to the disease was considerably weakened by the fact that these bacteria were also agglutinated by the sera of insane patients, not pellagrins, at Peoria and at Kankakee, and by the sera of apparently normal persons at Kankakee, Chicago, and Urbana, Illinois. Two of these bacterial strains, Nos. 14 and 67, appear to be identical in nature. The organism is a short rod about 4.0 μ long by 1.4 μ thick on the average. The size is variable, however, variations in length from 2.4 to 6.2 μ, and in thickness from 1.0 to 1.6 μ, being observed in young vigorous cultures. Gelatin is not liquefied. In litmus milk the organism grows without producing an acid reaction. There is slight coagulation after four days and a slow digestion of the casein. No gas is produced in broth containing dextrose, levulose, lactose, saccharose, or maltose. Fresh cultures on agar are colorless, but later assume an orange color, and this production of pigment seems to become more pronounced with continued artificial culture. Strains Nos. 14 and 67 agree in all these characters, and strain No. 35 in all except the pigment production. It has remained colorless. Inoculation of animals (guinea-pigs, rabbits, and monkeys) has been followed by loss of weight, but has not resulted in the death of any animal.

Further study along these lines has been undertaken by the Thompson-McFadden Pellagra Commission at the New York Post-Graduate Medical School during the summer of 1912. The opportunity was here presented to test this culture against the sera of pellagrins from a different part of the country, South Carolina. These recent cases have been divided into four series: First, 66 pellagrins showing lesions on the skin at the time the blood was taken; second, 43 pellagrins who did not show an eruption at the time but in whom a reliable history of the disease was obtained; third, 22 individuals living in the pellagrous district, Spartanburg County, South Carolina, but free from any sign or definite history of the disease; fourth, 27 individuals in New York, including clinic patients and some physicians who kindly furnished their own blood for this work. The agglutination tests were performed by the macroscopic method, a suspension of the bacteria in salt solution being mixed with an equal volume of a 20 per cent. solution of the serum in a small tube for each test, the final dilution of the serum being one part in ten. It was incubated for an hour and the progress of events recorded at intervals of fifteen minutes. Complete clumping and precipitation of the bacteria to the bottom of the tube was recorded as a complete reaction. Grades of almost complete, marked, slight, and negative were also distinguished. The results are shown graphically in Chart II.

Of the 66 sera in the first series, from pellagrins with the skin

eruption, 51 gave complete agglutination, 5 almost complete, 3 slight, and 4 negative reactions. The 43 sera of the second series gave reactions distributed as follows: complete 30, almost complete 6, marked none, slight none, negative 7. Of the whole 109 different sera from pellagrins, 74.3 per cent. gave complete agglu-

CHART II.—Results of agglutination tests.



Results of the agglutination tests. Complete reactions (1) in solid black at the left in each series; then in order (2) almost complete, (3) marked, (4) slight, and (5) negative reactions.

tination, 10.1 per cent. almost complete, 2.7 per cent. marked, 2.8 per cent. slight, and 10.1 per cent. negative reactions. The 22 sera of the third series, non-pellagrins of South Carolina, gave 5 complete agglutinations, 1 almost complete, 3 marked, 6 slight, and 7 negative reactions. The 27 New York controls gave 6 complete agglutinations, 3 almost complete, 10 marked, 1 slight, and

7 negative reactions. Of the total 49 controls, 22.5 per cent. gave complete agglutination, 8.2 per cent. almost complete, 26.5 per cent. marked, 14.3 per cent. slight, and 28.5 per cent. negative results. These findings are obviously not sufficiently clear-cut to warrant the assumption of a specific agglutination reaction of this bacterium with the serum of pellagrins, and yet they are such as to stimulate further work along this line.

The conservatism of this statement is not due to the fact that we have employed serum dilutions of one in ten instead of higher dilutions, for many of these positive sera have been tested in higher dilutions, up to one in four hundred, and have produced definite agglutination in such strength. The suggestion of specificity is, however, seriously opposed by the fact that sera from apparently normal individuals give precisely parallel results in some instances.

We have attempted to employ the complement-fixation test on a number of sera, using an antigen prepared from a culture of strain No. 67. Positive results have been obtained in a few cases, but it has not been possible to try it in a sufficient number of cases to determine the value of the test. We are also attempting to perfect a precipitin test. We hope that it may be possible, by employing these in conjunction with the agglutination test, to obtain more decisive results during the coming pellagra season.

A few cutaneous and intracutaneous tests on patients were performed during the year of 1912, using a vaccine made from a culture of strain No. 67. Of the 9 patients to whom the cutaneous test was applied, 1 gave a moderate reaction, 3 a slight reaction, and 5 were negative. The intracutaneous test on the same 9 patients gave a marked reaction in 1; a marked and a moderate reaction in another case in 2 tests; a slight reaction in 3 cases; a slight reaction and a negative reaction in another case in 2 tests; and a negative reaction in the 3 remaining cases; 2 controls gave negative results, one of them in two tests. The behavior of the cases, especially those on whom the test was repeated, seemed to suggest a difference in the reaction according to the stage of the disease, but the cases tested are still too few to bear analysis along this line.

While these various experiments with this culture were in progress we have undertaken to isolate further bacterial strains from the intestinal contents of pellagrins brought to New York for study. These cultures have been isolated by the methods previously employed, more especially by plating on blood-agar and ascitic-fluid-agar, from the feces, and also from the intestinal juice obtained through the Einhorn duodenal tube; 693 new bacterial strains were isolated in this way during 1912, and these have been tested against sera of pellagrins and others in approximately 2000 agglutination tests. This work is not yet completed, but it seems certain that we have failed to isolate any germ similar

to strain No. 67 from the feces of these new cases. From the duodenal fluid, however, a few strains have been obtained which have given positive agglutination tests with the serum of cases of pellagra, and which seem to agree in their biologic characters, so far as they have been tested, with strain No. 67.

It is evident that this phase of the investigation is in an unfinished condition, and we do not wish to draw any definite conclusions at this time. This report will give an idea of one of the avenues along which we have approached the possible bacteriologic phase of the problem of pellagra, and indicates one of the lines we hope to follow during the present year.

THE RATIONAL TREATMENT OF TETANUS, WITH A REPORT OF TWENTY-THREE CASES FROM THE EPISCOPAL HOSPITAL, PHILADELPHIA.[1]

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This paper is written with three purposes: (1) To report 23 consecutive cases of tetanus treated at the Episcopal Hospital, Philadelphia, during the last eight years; (2) by a review of the recent literature to endeavor to inculcate rational methods of treatment; and (3) in the hope that others may profit by our mistakes, as we have profited ourselves. For permission to record these case histories, as well as for the privilege of having under our personal care 11 of the patients, we desire to express our cordial thanks to the various members of the staff in whose services the patients were treated.

It is necessary first of all to inquire whether there is any such thing as a rational treatment for tetanus. We hold that treatment can be rational only when it is founded on a knowledge of the pathogenesis of the disease in question; and we believe that in the case of tetanus such knowledge exists.

Though previous generations had enough clinical acumen to class tetanus among diseases of the nervous system, and though the discovery of the Bacillus tetani by Nicolaier in 1884, and its isolation in pure culture by Kitasato in 1889, proved it to be an

[1] Read at a meeting of the Episcopal Hospital Clinical Society, November 18, 1912.

infectious disease, yet it is only within the past ten years that any definite knowledge as to its pathogenesis has been acquired. This knowledge has been secured almost solely through animal experimentation, and it is only as a result of the information gained in this way that rational treatment has become possible. Previous treatment, even if successful, was purely empirical. Especially noteworthy in the development of our knowledge have been the elaborate researches of Marie and Morax (1902), Meyer and Ransom (1903), Sawamura (1909), and v. Graff (1912). We have drawn freely from the various publications of these authors, as well as from Frazier's excellent critical review of the subject.

It is known that the disease is a pure toxemia. The bacilli or their spores may exist indefinitely in the tissues, and *no symptoms will be produced unless toxins are formed.* If the toxin is introduced into the system, it produces all the characteristic symptoms of tetanus even though no bacilli are present.

Experimental Tetanus. *Tetanus Ascendens.* In the small animals used in laboratory work the symptoms of the disease almost always begin in the inoculated extremity (*local tetanus*), and though other neighboring parts may become affected subsequently, yet trismus and retraction of the head almost never are observed, the disease being terminated by death or recovery before this stage is reached. In such animals (rabbits, rats, mice, frogs) if one lower extremity is inoculated with tetanus toxin the symptoms develop first and are most pronounced in that extremity; the opposite lower extremity is involved later, but not to the same extent; and when the spinal muscles become affected those of the injured side frequently are more involved than those of the uninjured side, thus resulting in pleurothotonos. The disease in such cases is known as Tetanus Ascendens; its symptoms develop first in the injured part and gradually ascend.

Tetanus Descendens. Usually in the larger animals and in man, in whom the disease is acquired not by the injection of toxin but by inoculation of the bacilli of tetanus, the symptoms begin first in the muscles of the neck and jaws, *no matter where the point of inoculation.* Subsequently the muscles of the back and trunk are affected, and finally those of the extremities, especially the lower extremities. The disease in these cases is distinguished as Tetanus Descendens. In man ascending tetanus is not extremely rare (Cases 2 and 4 of our series), though the initial symptoms (cramps and stiffness in the wounded extremity) often are overlooked, and the case is classed as one of pure descending tetanus. Mixed forms also exist, in which the disease seems to run both an ascending and a descending course.

Is there a satisfactory explanation for the difference between these two forms of tetanus, ascending and descending—the former being that which is produced experimentally, and the latter that which

occurs in nature? Zupnik in 1900 found that he could produce descending tetanus experimentally, even in small animals, provided the toxin was injected into muscle-free parts of the body, such as the tips of the toes (rabbits). These results were confirmed in 1909 by Sawamura, and it was he who advanced the true explanation for the difference between tetanus experimentally produced and that which occurs in nature. In experimental animals the toxin always had been injected into the muscular parts (usually the thigh or calf of the leg), and here it came into relation almost immediately with the motor nerves, was absorbed rapidly by them, and the part of the spinal cord first to be affected was that in anatomical relation with the wounded limb. In man, however, the usual point of inoculation is the hand or foot, and while a certain amount (perhaps a large amount) of toxin eventually reaches the nearest motor nerves and ascends them to the spinal cord, yet other portions of the toxin are taken up first by the lymphatics, then enter the general circulation, and passing out from the left heart are carried in short order to *the end-plates of all motor nerves throughout the body*. The portions of toxin reaching in this way the end-plates of such short nerves as those of the facial, cervical, and spinal muscles will reach the spinal cord through these short nerves, and will begin to produce tetanic spasm in the parts supplied by these short nerves, even before the toxin in the wounded extremity has had time to ascend the nerves of that extremity as far as the anatomically related region of the spinal cord. In this way, therefore, descending tetanus is to be explained. And Sawamura found that among 23 reported cases of ascending tetanus in man the point of inoculation was in a muscular part in every case but one, thus strengthening his view that the occurrence of ascending tetanus is due to the ready access of the toxin to the motor nerves. To prove this supposition still farther, he showed experimentally that if the nerves of an extremity are divided no local (ascending) tetanus can be produced by the injection of toxin; and that even if descending tetanus finally develops after many times the usual lethal dose of toxin has been injected, yet no local tetanus occurs in the enervated extremity.

Cephalic tetanus, as seen in man following wounds of the head or face, is to be explained in this way: It is a local tetanus, and it occurs first in the wounded part, and is manifested first by facial spasms and paralysis, because the toxin finds ready access to the short cranial nerves and reaches the centres which control them long before the toxin admitted to the general circulation reaches the spinal cord through other, longer nerve trunks.

Pathogenesis of Tetanus. 1. *The toxin ascends the peripheral nerves to the spinal cord.* From what has been said above it is evident that the symptoms of tetanus are due to the action of the toxin on the central nervous system, especially to its action on the

spinal cord.[1] It was shown by Marie and Morax in 1902, by Meyer and Ransom in 1903, and has been repeatedly demonstrated by experimenters since their time, and it may be accepted as irrefutably proved, that in ascending tetanus the toxin ascends the nerves of the wounded part (especially the motor nerves) until it reaches the spinal cord; that only when it reaches the cord does it begin to produce symptoms; that the first symptoms produced are in the parts supplied by the portion of the cord first attacked; that the toxin spreads in the cord, up or down, more especially ascending it; and that it produces symptoms in the parts supplied by every portion of the cord attacked. It is known that tetanus toxin can and does exist free in other portions of the body, such as the internal organs (liver, spleen), where it may be found after death; but that only those portions of the toxin which reach the spinal cord are able to produce recognizable symptoms.[2] And it is known that after death little or no toxin can be found in the spinal cord. At first sight this seems paradoxical, but the explanation is that when the toxin reaches the cord it soon enters into combination with the nerve tissue, becomes impregnably entrenched there, and cannot be dislodged by any known methods.

The peripheral nerves have little power of neutralizing the toxin —no more power than has the liver, for instance; and after death toxin may be recovered from the nerves as readily as from the internal organs. The peripheral portions of the nerves are found to give up more toxin than those portions nearer the spinal cord. In other words, *the nearer the toxin gets to the spinal cord the more impregnably entrenched does it become in the nerve tissue.* A much larger amount of toxin must be injected into the periphery of the limbs (*e. g.*, subcutaneously in the toes) to cause death, than in the central portions of the limbs (*e. g.*, intramuscularly); in other words, *the readier the access of the toxin to the central nervous system the less is the amount required to kill.* The minimal lethal dose is much less if injected into a nerve than if injected anywhere else; it is less when injected intramuscularly than if injected subcutaneously or intravenously.

The *incubation period* depends on the distance from the cord of the site of injection of the toxin. If the toxin is injected into one of the lower extremities of a rabbit, the first definite symptoms appear about the third day; if the injection is made into the subdural space of the cord, or into the cord itself, the incubation period is only a few hours. Division or resection of nerves after intramuscular injection of toxin could save the lives of rabbits only if done within about one hour of the time of injection of the toxin; but even in fatal cases life was

[1] In animals rapid emaciation sometimes has followed administration of tetanus toxin, when no tetanic symptoms were produced. Probably these cases, which are described as *tetanus sine tetano*, are due to the action of the toxin on structures other than the nervous system.

prolonged more than when the nerves were not cut, no matter if an interval of from eighteen to forty hours elapsed between the injection of the toxin and section of the nerves of the limb (Sawamura). The use of cocaine in the afferent nerves, or the division of all sensory nerves (leaving the motor nerves intact) may retard the development and diminish the severity of the course of tetanus, but it cannot prevent it. The same is true of intradural division of the posterior nerve roots (Sawamura). If local tetanus has not lasted long, it can be stopped by section of the nerves or by use of curare; but if it has lasted over two days, the tetanic muscle cramp will not be influenced by these methods and will persist even after death. According to Gumprecht this is to be explained as a fatigue phenomenon, commonly seen in physiological experiments; he never found reactions of degeneration present.

By what structures of the nerve does the toxin reach the cord?

Gumprecht (1894) and Stintzing (1898) claimed that it went only through the peri- and endoneurium, passing thence mostly into the cerebrospinal fluid, but also entering directly into the spinal cord, though in smaller amounts. In support of this theory, Gumprecht found that if he injected toxin into the subdural space of the cord in the lumbar region, local tetanus began first in the animal's hind legs. Stintzing found that the cerebrospinal fluid of two men, very ill with tetanus, was very toxic for mice, while the blood of these patients was not toxic. But Meyer and Ransom (1903) repeated Gumprecht's experiment, and found, if care was taken not to wound the pia or the cord, that general (descending) tetanus was produced before local (ascending) tetanus; moreover, they did not find the cerebrospinal fluid toxic either in patients or experimental animals. These latter investigators (l. c., Obs. 32, S. 413) injected a moderate amount of toxin into the sciatic nerve of a highly immunized rabbit, and nevertheless fatal ascending tetanus developed; yet examination showed that the blood, the cerebrospinal fluid, and the nerve lymph contained active antitoxin. The amount of antitoxin in the nerve lymph, however, was very small—very much less than that in the blood. A twenty-five-fold lethal dose of toxin had been without effect when injected subcutaneously, because at once neutralized by the antitoxin in the circulating blood; two drops of the blood contained more than enough antitoxin to neutralize the fatal dose of toxin injected into the nerve. Their conclusion was that the toxin when injected into the nerve must have reached the cord by way of the axis cylinders, since the antitoxin in the nerve lymph could not neutralize it; but it seems to us an equally correct conclusion that the amount of antitoxin in the nerve lymph was insufficient, even if that in the blood was superabundant. Further reference to this question is made in connection with the prophylactic use of antitoxin (p. 817).

All that it seems safe to conclude is:

1. The toxin surely ascends the nerves by way of the axis cylinders (perhaps by means of a centripetal protoplasmic current), and in this way can produce a severe tetanus ascendens.

2. The transmission of toxin through the peri- and endoneurium cannot be excluded, and the toxin absorbed in this way may play an important part in the development of local tetanus.

The above facts, briefly outlined, are those which prove that the toxin ascends the peripheral nerves to the cord.

2. *The toxin spreads to neighboring parts of the spinal cord.* The diffusion of the toxin in the spinal cord has been demonstrated in several ways. Marie and Morax injected toxin into the lumbar swelling of the cord, and thereafter found toxin in the dorsal cord. If the cord is cut through above the lumbar swelling, tetanus develops only in the lower extremities in cases where toxin has been injected previously into the sciatic nerves, and no tetanus develops in the parts supplied by the cord above the point of section. Moreover, the usual sequence of symptoms in ascending tetanus bears witness to the gradual spread of the toxin within the spinal cord—first the wounded extremity becomes tetanic, then the other lower limb; next the back and abdomen, then the fore limbs, and finally, the neck and head.

Invasion of the sensory portions of the cord also occurs, and is responsible for the extreme hyperexcitability, evidenced by the facility which very feeble peripheral stimuli possess of causing severe clonic convulsions during the disease. If the toxin is injected experimentally into the sensory nerves it is blocked effectually by the ganglia on the posterior roots; if injected into the posterior roots on the proximal side of the ganglia, a very painful form of the disease, termed Tetanus Dolorosus, is produced; and the animals die of exhaustion before the motor phenomena, so characteristic of the disease in its ordinary forms, have had time to develop.

3. *Some of the toxin enters the general circulation.* This is proved primarily by the fact that toxin has been found in the blood on numerous occasions, in experimental animals and in man. It was first found in the blood of man by Nissen in 1891.[3] *This toxin eventually reaches the cord and produces descending tetanus.* This is proved, because even after all the nerves of a limb have been cut, tetanus descendens can be produced by injecting toxin into the enervated extremity, though many times the usual lethal dose is required. It is certain that the toxin reaches the cord from the general circulation chiefly, if not only, by being brought into contact first with the end-plates of the various motor nerves, and by

[3] According to Stintzing, however, it could not be demonstrated in the blood by Rosenbach, Schulz, Billroth, Moritz, Henoch, and Engelmann.

being transferred through these nerves to the cord. This occurs even when the toxin is injected intravenously, but at present it cannot be certainly proved that no toxin reaches the central nervous system *directly* by the blood; but it seems highly improbable.

Morbid Anatomy of Tetanus. Thus far it has not been possible to find, in the peripheral or central nervous system, or elsewhere, any changes which are specific for tetanus. There may be swelling and fragmentation of the axis cylinders, and hemorrhages with vacuolation of the cells in the anterior horns of the spinal cord; but these changes cannot be distinguished from those due to other causes. The recovery of the Bacillus tetani from the point of inoculation often is impossible, and scientific confirmation of the diagnosis must rest in many cases upon the reproduction of tetanic symptoms in animals by the injection of toxin extracted from the patient. In the vast majority of cases the clinical diagnosis is quite certain enough without any confirmatory evidence from the laboratory.

Of 15 cases studied bacteriologically, Huber reports that the Bacillus tetani was recovered from the wound in 8. This seems a larger proportion of successful cultures than in most series of cases. In our own series of 23 cases, search was made only in a few instances, but never was successful.

In 2 patients, in whom the wound was in the lower extremity, Porter and Richardson excised the inguinal lymph-nodes, and in both cases found tetanus bacilli in the nodes.[4] This demonstrates that the bacillus does not, in all cases, remain in the immediate vicinity of the point of entrance, and suggests that the persistence of symptoms of toxin absorption even after wide excision or amputation of the primary focus may be due to toxin elaborated by bacilli lodged in the anatomically related lymphatics.

Cause of the Symptoms of Tetanus. The toxin stimulates the motor cells of the spinal cord, with the result that the muscles controlled by these cells are thrown into tonic spasm; the toxin, as already noted, also renders the sensory side of the cord extremely susceptible to external stimulus, so that very insignificant stimuli, such as the slamming of a door, jarring the patient's bed, a sudden draught of air, etc., will bring on clonic convulsions, or at least will greatly intensify, for the moment, the tonic spasms.

Therapeutic Indications. These may be summarized as follows:

1. To prevent the development of tetanus.
2. To remove the source which supplies the toxin, *i. e.*, the bacilli of tetanus.
3. To head off and neutralize the toxin already formed.

[4] Schnitzler had found the bacilli in the inguinal lymphatics at autopsy, and Fricker also had found them in the related lymph-nodes.

4. To depress the functions of the spinal cord.

5. To sustain the life of the patient by proper nourishment, nursing, etc.

PROPHYLAXIS OF TETANUS.

It is well known that *certain classes of wounds*, received in certain surroundings, are more often followed by the development of tetanus than are ordinary wounds. The Bacillus tetani is anaërobic, and is found especially in garden soil, barn-yards, stables, etc. Probably it normally infests the intestinal tract of horses and cattle, and is deposited with their dung. So long as the mucosa of their gastro-intestinal tract is intact, they are not liable to infection by this channel, on account of the antitoxic properties of the intestinal juices, especially the bile (H. Vincent). Matas suggests that postoperative tetanus may be due to tetanus bacilli, latent in the patient's intestinal tract, ingested with uncooked food, and infecting the operative wound by fecal contact. There is no good evidence that it is due to the use of infected catgut. According to Fox, tetanus bacilli are found in the feces of 5 per cent. of mankind; and in the feces of 20 per cent. of men who work about horses.

On these accounts, wounds received by farmers, gardeners, stablemen, etc., are especially liable to be infected with tetanus bacilli. Wounds by farming or gardening implements; wounds by axes, as in felling trees; machinery crushes; wounds produced by dragging in the dust, by kicks or bites of horses; wounds by nails, spikes, etc., incrusted with dirt and rust—these are the causes most to be feared.

In our own series of 23 cases, there were 10 in which the wound was contaminated by country earth or street dust; 2 caused by splinters from the floor; 5 by rusty nails or iron spikes; 3 due to machinery accidents; and 1 each to a gunshot wound, puerperal infection, and an explosion.

Inoculation is favored by *anaërobic conditions of the wound*. Especially favorable sites are wounds in which the tissues are sloughing; the best culture medium for tetanus bacilli, according to Tarrozzi, is that which contains some dead organic tissue. Thus punctured wounds, contused and lacerated wounds, and wounds in which there are foreign bodies (earth, machine oil, splinters, wadding, etc.), offer favorable conditions for the development of any bacilli present. A mixed infection, especially with saprophytic bacteria, is favorable because these organisms, being aërobic, absorb all available oxygen and provide anaërobic conditions for the tetanus bacilli.

Care of the wound is naturally the first step in the prophylaxis of tetanus. Such wounds as are considered to offer favorable soil for the development of tetanus bacilli should be treated with even

more than ordinary antiseptic precautions. If the original wound is properly treated, the development of tetanus is unusual. Of our own 23 patients, only 7 had received proper treatment of the wound; and, even in these 7, extra precautions not adopted no doubt would have been taken if the possibility of the development of tetanus had been kept in mind. It is our firm belief that efficient care of the wound as soon as possible after it is received is by all means the most important feature in prophylaxis. We have never yet had a case of tetanus develop in a patient whose wound has been under our care from the first.

Here we must call attention to Case 11 of the present series. This patient was seen by both of us in the Out-patient Department a few hours after his injury was received. Recognizing the gravity of the wound, we referred him at once to the ward of the hospital. Unfortunately he was permitted to return home almost immediately, without proper treatment of the wound, and ten days later developed acute tetanus, from which he died. Efficient treatment of the wound at first might have altogether prevented tetanus, or at all events might have lessened its severity.

Our method of treating a suspected wound is as follows: (1) The surrounding skin is painted with a 3 per cent. alcoholic solution of iodine. (2) Then *all parts of the wound are made accessible*, by wide incision if necessary. (If a punctured wound of the foot, of suspected nature, exists, it is freely opened to its depths, dividing the plantar fascia as far as necessary. If the patient lives far from the hospital, and cannot return home on crutches, he is kept in the ward.) (3) The wound is mechanically cleansed by scissors and forceps, and then is thoroughly swabbed out with the iodine solution. (4) The wound is lightly filled with gauze soaked in the iodine solution, and is properly dressed. We *avoid all caustics*, as they kill the tissues, and the resulting sloughs, even if minute, furnish favorable sites for the growth of tetanus bacilli. At subsequent dressings (daily at first) the wound is exposed by removal of the iodine gauze, is irrigated with peroxide of hydrogen until active effervescence ceases, and is again filled with gauze soaked in the iodine solution. This method of dressing is continued until healthy granulations are formed. Bockenheimer has concluded from experimental work that the best dressing for these wounds is Balsam of Peru which he believes is antibacterial to the tetanus bacilli. Hessert commends this dressing.

The Prophylactic Use of Antitoxin.[5] This was first extensively employed in veterinary practice by Nocard, in 1895, and is found

[5] For the following information we are indebted to Dr. A. Parker Hitchens, of Glenolden, Pa.: The United States Government has established a standard method for testing the strength of tetanus antitoxin: "The immunity unit for measuring the strength of tetanus antitoxin shall be ten times the least quantity of antitetanic serum necessary to save the life of a 350-gram guinea-pig for ninety-six hours against the official test dose of the standard toxin furnished by the Hygienic Laboratory of the Public Health and Marine Hospital Service." The official

to be almost of absolute value. That it is not by any means always effective when used in man, is only too well known. The reasons for the difference in its action in horses and in man must depend, as pointed out by Solieri, on one of two factors: either it is not so useful or it has not been properly administered. (1) Perhaps the fact that horses (in which its use is most successful) are treated by antitoxin derived from their own serum, while human patients are treated by an alien serum (horse), makes the difference. But to this supposition (and it is little more) it may be replied that other animals, such as cattle and sheep, are well protected by the horse serum. (2) The most reasonable explanation of the numerous failures of antitoxin to prevent the development of tetanus in man lies in the faulty manner in which it has been administered, in most cases. Remertz has tabulated 55 cases where tetanus developed in spite of the prophylactic use of antitoxin; in 38 of these cases the diagnosis is positive; and as only 30 of these patients died (53 per cent.) it is evident that the antitoxin at least rendered the disease less fatal; but even with all allowances the mortality in these cases cannot be brought below 40 per cent.

There are three things to be considered in the matter of the prophylactic use of antitoxin: (1) The frequency with which it should be given. (2) The site of the injection. (3) The quantity to be administered.

1. *The frequency of prophylactic injections.* It appears to be a well-ascertained fact that the antitoxin is all eliminated from the system in about eight or ten days after the injection. It remains in practically undiminished amount for a week, and then rapidly diminishes to nothing in the course of two days (Dehne and Hamburger). As the tetanus bacilli, if any are lodged in the wound, may not begin to produce any toxin until at least as long a time

test dose of toxin is one hundred times the smallest quantity of toxin which will kill a guinea-pig within ninety-six hours. Dr. Hitchens adds that Rosenau and Anderson (1908) found in a German serum which they examined 330 units per c.c., and in some French serums from 40 to 66 units per c.c. Dr. Hitchens examined some French serums in 1910, and found they contained from 30 to 50 units per c.c. He permits us to publish the following results of other examinations made by him in 1910. He thinks that the tests may have been a little too rigid, and that the results noted below are about 15 per cent. too low.

Behring (5 fach.)	220 units per c.c.
Behring (5 fach.)	200 units per c.c.
Berne	12 units per c.c.
Höchst (4 fach.)	110 units per c.c.
Höchst (5 fach.)	250 units per c.c.
Krakau—less than	1 unit per c.c.
Vienna	120 units per c.c.
Lister Institute (veterinary)	30 units per c.c.
Rebman, London, less than	1 unit per c.c.

If the serum at present in use in these countries remains as weak as in these samples, it is evident that the doses of antitoxin administered abroad for therapeutic effect have been quite insufficient. In this country tetanus antitoxin is supplied in tubes each of which holds 10 c.c., the strength being 1500, 3000, or 5000 units per 10 c.c. according to the concentration.

as this has elapsed, it is manifestly important, if the antitoxin is to be of use, that some should be present in the system for two or three weeks after the receipt of the injury. In many cases the tetanus bacilli do not enter the wound at the time of the accident, but are introduced secondarily by the carelessness of the patient in neglecting to return for dressings, and in attempting to care for the wound in septic surroundings at home; in such cases surgery can scarcely be held responsible. But even if present in the wound from the first, the bacilli may lie dormant for weeks in spore form, before development occurs with the production of toxin.

Vaillard cites 6 cases in which the period of incubation was over a month, in 1 of which (Terrier) it was eighty-seven days. In Case 4 of our series, with an incubation period presumably of eight weeks, the onset was very gradual, but the disease then developed in frightfully acute form and was rapidly fatal. Fox says that tetanus spores injected into a guinea-pig have remained latent for four months, and have then, without apparent cause, produced an outbreak of the disease. In some such manner as this, no doubt, are to be explained the not very unusual cases where the symptoms of tetanus recur some time after apparently complete recovery from a frank attack of the disease. Fink reports two severe relapses at intervals of several months, due to the development of latent spores; Fedden records such a case, where symptoms recurred over one month after complete recovery; and Reynier narrates a rather mysterious case where slight recurrent attacks of tetanus occurred throughout a period of six years, and in which finally a typical and very severe attack occurred, apparently caused by the hypodermic injection of a quinine salt.[6]

The necessity for a second injection of antitoxin about the eighth or tenth day is thus very evident, and it may be well to administer a third injection during the third week. Solieri insists that this injection must be renewed every eight or ten days until all necrotic tissues are removed and there is a clean granulating surface. In almost all of the 55 cases, noted above, in which tetanus has developed in spite of the prophylactic use of antitoxin, *the injection was not repeated.*

But that even repeated injections may prove ineffectual is demonstrated by the well-known case recorded by Maunoury: 10 c.c. of antitoxin was injected at once after the injury; this was repeated in six days; and again six days later a third injection was given. Twelve days after the third injection, as the patient complained of severe pain in the wounded part, a fourth injection was given, and the limb was amputated. In spite of this, three days later (twenty-seven days after injury) tetanus developed,

[6] Subcutaneous or intramuscular injections of quinine salts may arouse latent tetanus spores, because they cause local necrosis (Vincent, 1904). This subject is well discussed editorially in the Indian Medical Gazette (1911, xlvi, 141 to 142). This teaching is controverted by Palmer and by McCampbell; the latter holds that quinine can be held responsible only if there is already present a secondary (pyogenic) infection.

and the patient died of severe tetanus in twenty-four hours. (Was this possibly a case in which some bacilli had lodged in the lymp nodes, or was it that the antitoxin injected at the end of the second period of six days had all escaped from the body at the end of the next twelve days, when the fourth injection was given?).

2. *The site of the injection.* In most of the reported cases no details of the site of injection are given, but in such cases it is presumed that the antitoxin was administered subcutaneously.

Calmette, and later McFarland, applied antitoxin in powdered form directly to the wound, in experimental prophylaxis, and found it of great value. Lop, however, found it did not prevent the development, eight days after injury, of tetanus fatal in three days, though the wound was powdered with antitoxin one-half hour after the injury, and again three days later. Luckett had a similar experience. It may be, as suggested by Tuffier, in the discussion of Lop's case, that the antitoxin was absorbed by the dressings applied instead of by the wound. Remertz refers to two other cases in which the use of powdered antitoxin proved ineffectual.

The subcutaneous use of antitoxin in prophylaxis is open to the same objections raised against this method of therapeutic administration (*q. v.*). In any circumstances the antitoxin should be given as near to the wound as possible, so as to flood the tissues in the immediate vicinity; and the injection should be deep, intramuscular if possible, so as to permit its rapid absorption by the motor nerves. If the antitoxin can reach the peripheral nerves before any toxin that is formed reaches them, the likelihood that the toxin ever will reach the spinal cord is much decreased. If any nerves are exposed in the wound the antitoxin should be injected into them.

This was the idea of Meyer and Ransom, who thought the imperilled spinal-cord centres might be protected from the toxin by blocking the afferent nerves with antitoxin. They proved that if one sciatic nerve of a rabbit was injected with antitoxin, and simultaneously both legs below the knees were injected with toxin, then only the protected limb remained free from tetanus or developed it very late. Sawamura repeated these experiments: first he injected twice the lethal dose of toxin in the leg, and from sixty to ninety minutes later injected antitoxin into the sciatic nerve of the same limb; 6 out of 8 rabbits thus treated did not die, and the limb so treated remained free from local tetanus in all, even in the 2 fatal cases where death was caused by general tetanus. The 6 control animals (not protected by antitoxin in the nerve) all developed local tetanus, and 2 died of general tetanus.[7]

[7] The fact that intraneural injections of antitoxin block the further progress of toxin along the nerves, is good evidence, it seems to us, either that the toxin ascends in large amounts through the lymph channels of the nerves, or that antitoxin can be readily absorbed by axis cylinders which are in its neighborhood. It evidently is not necessary for the injecting needle to penetrate each and every axis cylinder of the nerve trunk.

If antitoxin was injected subcutaneously or intravenously, even in two or three times the quantity, it was powerless to prevent the development of local tetanus. The experiments conducted by v. Graff, to test the prophylactic value of antitoxin administered intravenously, are detailed below.

3. *The quantity of the injection.* Usually 1500 units is the amount employed as a prophylactic dose. Remertz thinks that even if the injection is made very soon after the injury, the least amount that can be useful as a prophylactic dose is from 2 c.c. to 5 c.c. (= 20 A. E.); according to Hitchens' table (p. 815) this is equivalent to about 1500 units, U. S. A. Remertz says that Lotheisen thought 100 A. E. was the proper prophylactic dose. Taking the average weight of persons injected as 150 pounds, and figuring out the potency of the antitoxin from the known value of a unit (U. S. A.), we find that 1500 units is a little over two thousand times the amount necessary to neutralize the minimal lethal dose of toxin in such an individual. Such an amount is by no means excessive, in view of the fact that the amount of antitoxin required to prevent death increases in geometrical progression with the lapse of time. After the lapse of one hour, twenty-four times as much antitoxin is required as when antitoxin and toxin are injected simultaneously (Remertz). Certainly antitoxin will be more useful if injected in the immediate neighborhood of the wound than elsewhere, as it will then be in more concentrated form as it comes into relation with the forming toxins.

Objections to the prophylactic use of antitoxin. The chief objection is the expense. Unpleasant symptoms from its use are scarcely known, even when it has been used in massive doses as a therapeutic measure. The site of the injection often is painful, and if carelessly given, harm may result.

We are cognizant of one case where the injection was made by a trained nurse, by order of a physician. The needle was introduced on the outer side of the thigh, but too near the knee; the result was that the antitoxin was injected into the subfemoral bursa, and the patient was laid up in bed for several days, with "water on the knee."

Occasionally, in susceptible individuals, an erythematous or urticarial rash develops and multiple arthritis has been reported (Reynier), but other evidences of anaphylaxis do not appear to have been observed.[8]

In conclusion, it may be said that the worst reproach that can be made against the prophylactic use of antitoxin is that, while it is harmless when carefully administered, it may be useless. That it never is useful has not been proved; and we believe that so long

[8] Riche has recorded a death following the prophylactic injection of tetanus antitoxin in a patient under the care of Rilhac; but the *cause* of death was undetermined.

as a possibility of its usefulness exists, it is proper to employ it in the case of suspected wounds. In none of the patients in our series had a prophylactic injection been given. At least 1500 units should be given, in the immediate neighborhood of the wound; it should be injected deeply into the muscles; or if possible, into the nerves (when a smaller quantity will suffice). This injection *should be repeated* at the end of seven or eight days; and, if possible, a third injection should be given during the third week.

Finally, a few words may be said about "*Fourth of July Tetanus.*" In spite of diligent, and we believe unprejudiced, study of the subject, we have been unable to convince ourselves that such injuries received on "the day we celebrate" are more liable to be followed by tetanus than other contused or lacerated wounds.

During the years one of us was on duty at the Children's Hospital, Philadelphia, where many such cases were treated every year, antitoxin never was employed as a prophylactic (the hospital being unable to afford it), but the wounds were cleansed as above described with most meticulous exactitude; yet not one case of tetanus due to such an injury ever occurred. Indeed, we have never seen anywhere a case of tetanus due to such an injury.

We believe, however, that the campaign for the use of antitoxin as a prophylactic has accomplished a marked reduction in the incidence of tetanus; but we hold that this result may be attributed as rationally to better care of the wound as to the antitoxin employed, because a physician who thinks of antitoxin thinks also of tetanus, and the thought of possible tetanus impels him to take proper care of the wound. Moreover, in only an extremely small proportion of cases has the injection been repeated.

(To be continued.)

THE OCCURRENCE OF CANCEROUS CHANGES IN BENIGN NEWGROWTHS OF THE SKIN.

By Richard L. Sutton, M.D.,

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In many instances the line which separates malignant from non-malignant cutaneous tumors is a shadowy one. Heidingsfeld,[1] in a comparative histologic study of 5 cases of "benign cystic epithelioma" (one of which, judging from the slides exhibited, was an example of syringocystadenoma), and one each of morphea-like epithelioma and carcinoma epitheliale cicatrisans, has expressed the opinion that all growths of the Brooke[2] type are premalignant

[1] Jour. Amer. Med. Assoc., lix, 256.

[2] British Jour. Dermat., 1892, p. 269.

in character and structure. While few pathologists will agree with Heidingsfeld in this assertion, the fact remains that in a few instances, as in the cases of multiple benign cystic epithelioma reported by J. C. White,[3] Jarisch,[4] Stelwagon,[5] and Dennie and myself[6] there has been a concomitant epitheliomatosis of the rodent ulcer type.

McDonough[7] has recently made an interesting and valuable contribution to the pathology of the skin from the eyelids and the nasofacial grooves. He takes the view that the majority of tumors affecting the orbitofacial and nasofacial grooves are of epithelial origin, and atavistic of both the lower eyebrows and the specialized glands found in these regions in many of the mammalia, and believes that all of the growths, from a simple lanugo hair follicle to a rodent ulcer, are links in one chain, the former being the head or most mature, the latter the tail or most embryonic. As they are all links, the histologic differences of any one clinical entity are at once apparent. This explanation is exceedingly plausible, particularly as regards the relative frequency of growths in this region; but unfortunately it does not go far enough. While tumors of the various types included (adenoma sebaceum, acanthoma, or epithelioma, adenoides cysticum and its subvariety, tricho-epithelioma of Jarisch, "syringoma," and rodent ulcer) are often found in the areas indicated, in the majority of instances their distribution is much wider, and, in several of the cases reported, the eyelids and nasofacial grooves were not involved at all.

Adamson,[8] in discussing 2 cases of multiple rodent ulcer, gives an admirable and concise review of the subject in general, and discusses the possible interrelationship of rodent ulcer, multiple rodent ulcer, and acanthoma adenoides cysticum with and without accompanying manifestations of malignancy. He points out the features possessed by all of the growths in common—derivation from the basal layer of the epidermis or from the hair follicle, occurrence of the growth in the form of cell masses having a palisade marginal layer and a centre of rounded or oval cells, the tendency to cyst formation, and the presence of a newly formed capsule of connective tissue surrounding the epithelial masses. For contrast, he emphasizes the highly vascular character of the fibrous elements in the lesions of rodent ulcer, together with the plasma-cell exudate at the advancing margin of the growth, and the ever-present tendency of the outlying groups of epithelial cells to invade the tissues beyond the main body of the tumor.

[3] Jour. Cutan. Dis., 1894, p. 477.
[4] Arch. f. Dermat. u. Syph., 1894, p. 164.
[5] Diseases of the Skin, Philadelphia, 1910, p. 634.
[6] Jour. Amer. Med. Assoc., lviii, 333.
[7] British Jour. Dermat., 1912, p. 291.
[8] Lancet, London, clxxv, 1133.

As Adamson succintly states, "histologically the legions of rodent ulcer have many features in common with those of epithelioma (acanthoma) adenoides cysticum, and they are probably derived from the same part of the epidermis. Pathologically they differ n that the one tends slowly to invade and to destroy the surrounding tissue, while the other has no such tendency."

For several months I have had under observation two unusual cases of rodent ulcer, the histories of which are of interest in relation to this subject.

FIG. 1.—Case I. Acanthoma adenoides cysticum, showing size and distribution of tumors.

CASE I.—A. G., female; married; housewife; aged fifty-one years. This patient has been under the care of my friend, Dr. Oliver H. McCandless, a Röntgenologist of Kansas City for the past four or five years, and it is with his permission that the history is here given.

Family History: So far as the patient is able to discover, only one other member of the family, a daughter, has ever had a similar cutaneous disorder.

Personal History: The patient is a native of Indiana, and a resident of Rosedale, Kansas. Her health has always been good. She has never had a skin disease other than the one from which relief is now sought.

Present Illness: When the patient was about fifteen years of age, several small discrete papular growths appeared on her face and back. The lesions were thought to be warts, and little attention was paid to them. In course of time the tumors increased in

number, until in 1906 there were more than seventy of the lesions, varying in size from a millet-seed to an English walnut, asym-

FIG. 2.—Case I. Rodent ulcer of inner angle of left eye. Acanthoma adenoides cysticum on face and forehead.

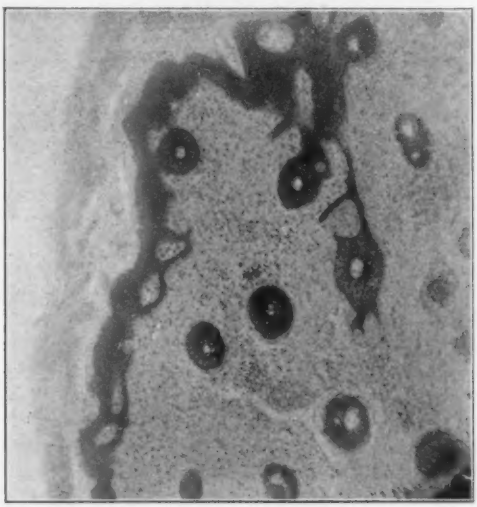

FIG. 3.—Showing histologic features of a typical tumor in acanthoma adenoides cysticum.

metrically distributed over the face, neck, and chest. The majority of the tumors were mushroom-shaped, with a short pedicle and a shiny, button-like top. In 1907 one of the growths was excised and examined microscopically by Dr. Frank J. Hall. It was found to be a typical acanthoma adenoides cysticum of Brooke.

Prior to the case coming under the care of Dr. McCandless some of the lesions had been curetted, cauterized with acids, or treated with an electric needle. Since the patient has been in his charge, dependence has been placed for the most part on the *x*-rays. About one year ago a small cystic tumor appeared at the inner canthus of the left eye, at a point where, so far as known, no lesion had previously existed. In the course of a few weeks this tumor broke down and an ulcer developed, clinically indistinguishable from an epithelioma. Despite treatment this ulcer has continued to increase in size.

Examination: The patient is a well-preserved woman, with brown hair and eyes. Irregularly scattered over the face, neck, and trunk are sixty or more solid tuberous growths, varying in size from a pin-head to an ordinary checker. Many of the lesions are tender on pressure, although only a few show evidence of the presence of inflammation. Several scars, the sites of lesions that have been removed, are to be seen on the forehead and chin. At the inner angle of the left eye, and extending downward to the ala of the nose, is a superficial ulcer, triangular in outline, with rounded, shiny, indurated borders. Permission to perform a biopsy was refused. Although some of the nodular lesions showed inflammatory or ulcerative changes it is probable that these were coincident with healing, and were the result of treatment.

Case II.—L. T.; female; married; housewife; aged twenty-three years. This patient was first admitted to Professor Walter S. Sutton's service (surgical) at the University Dispensary, and later was referred by him to the dermatologic department for observation and treatment.

Family History: This patient is the daughter of the woman whose case history has just been given. She also has a daughter, three years of age, but the child's skin is free from lesions of any kind.

Personal History: The patient is a native and a resident of Wyandotte County, Kansas. Her general health has always been excellent.

Present Illness: In August, 1905, the patient first noticed the presence of several small, flat-topped "moles" on her forehead, face, and neck. The little tumors were pink in color, painless on pressure, and irregularly distributed over the affected areas. Since that time a new papule has occasionally appeared, the older ones, with a single exception, having ceased to increase in size after they had attained the diameter of a grain of wheat. In

the exception noted the lesion, which was located on the right side of the neck, near the hair margin, broke down, in January, 1911, and the resulting ulcer gradually increased in area until it was a centimeter or more in diameter. The margin was elevated, nodular, and pearly, and, when the growth was excised, by Dr. Walter Sutton, in December, 1911, it was found to be a typical rodent ulcer.

FIG. 4.—Case II.—Multiple rodent ulcers, showing size and distribution of lesions.

Examination: The patient is a brunette, with brown hair and eyes. On parts other than the face and neck her skin is smooth and unmarked. The texture of the skin of the face is somewhat coarse, and there are present, even in the winter time, large numbers of freckles. The integument is soft and pliable, however, and there is no suggestion of xeroderma. Scattered irregularly over the forehead, face, and neck are a number, fifty-two in all, of small, flat, or round-topped, somewhat burnished, flesh colored papules, varying in size from a millet-seed to a large grain of wheat. The little nodules are firm to the touch, and painless on pressure. None are broken down or ulcerated. Three of the lesions were

excised by means of a small cutaneous punch, under cocaine anesthesia, and examined microscopically. All three were similar in structure, typical epitheliomas of the rodent ulcer type, the proliferating elements being derived from the basal layer of the epidermis.

FIG. 5.—Case II.—Showing histologic features of a characteristic lesion.

TREATMENT. Practically all of the remaining tumors have been removed by means of Pusey's carbon dioxide snow. The method is almost painless, and proved exceedingly efficacious, only a small depressed scar remaining to mark the site of each former growth. The comparatively slight amount of irritation resulting from the application of this agent renders it far preferable to the needle or to chemical caustics or the curette in cases of this character. More than a year has elapsed since the first growths were removed, and no untoward symptom of any kind has developed.

While it is hardly probably that the presence of acanthoma adenoides cysticum in the first case here reported had any direct bearing upon the subsequent appearance of the rodent ulcer, the fact that the patient's daughter developed tumors of a malignant type is exceedingly suggestive of a more than casual connection between the two conditions. Judging from a fairly exhaustive study of three different cases of acanthoma adenoides cysticum, I believe the lesions to be embryonic in origin, and similar, in some respects, to those of syringocystadenoma. The evenness and

regularity with which the epidermal processes extend into the adjacent connective tissue, the retention of many of the characteristic contoural and tinctorial qualities of the epithelial elements, the freedom from associated plasma-cell infiltration, and in the vast majority of instances the total absence of malignant tendencies of any kind all point to the correctness of this hypothesis.

On the other hand, in rodent ulcer and allied types of epitheliomas one of the most distinctive and striking features is the apparent freedom of the growth from guidance or restraint of any kind, and the manifest insatiable desire of the constituent cells to tear down and destroy normal structures with which they come in contact.

Although the parasitic nature of malignant growths in man is as yet unproved, the result of the investigations of Erwin F. Smith[9] and others on a strikingly similar disease in plants ("crown gall," due to the bacterium tumefaciens) is encouraging, and it is probable that the discovery and isolation of the causative organism, or organisms, is only a matter of time. Certain states and conditions of the skin undoubtedly predispose to attacks of this kind, and a suitable soil may be inherited as well as acquired. That the changes occasioned by the presence of such an affection as acanthoma adenoides cysticum renders the skin more susceptible to cancerous involvement, however, I consider improbable, and unproved by the evidence now at our disposal.

THE USE OF ANTITYPHOID VACCINE DURING THE COURSE OF AN EPIDEMIC.[1]

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Previous Reports. The use of antityphoid vaccine in military and civil life, particularly in institutions, has been carefully studied. The statistics which have been compiled have presented most prominently the types of local and general reactions observed, the strains of microörganisms used, and, to a much less extent, studies upon agglutinins, bacteriolysins, phagocytosis, and some rather insufficient references to the "negative phase."

However, records of its use as a prophylactic agent during the course of epidemics have been meagre. The earliest record is that by Cullinan, of Dublin (quoted by Wright[2]), who reports inoculations of over 500 persons during an epidemic lasting five months

[9] Moore, Jour. Cutan. Dis., 1912, p. 515.

[1] Read in the Section on Medicine of the College of Physicians of Philadelphia, April 28, 1913.

[2] British Med. Jour., October 26, 1901, p. 1226.

in the Richmond Asylum. Among those inoculated only 1.35 per cent. contracted the disease, all of whom were in the incubation stage of the disease at the time; 14.9 per cent. of 114 uninoculated nurses subsequently developed typhoid fever. Leishman,[3] Wright, and Semple inoculated 100 attendants in the Barming Asylum during the Maidstone epidemic in 1897; none of those vaccinated developed the disease.

It was used extensively in an epidemic in Torrinton,[4] Connecticut, during the summer of 1911, only one case occurring among those vaccinated. Russell[5] mentions its use during an epidemic in Cuba in which 2500 marines were subject to exposure, and again in Cedar Rapids, Iowa, during 1912. Ravenel[6] refers to its use during an epidemic in a small Wisconsin town during the same year. Vincent[7] reported the results obtained by him in Algiers and Morocco. However, as was subsequently pointed out by Metchnikoff,[8] the disease was endemic and not epidemic in the countries in which Vincent's studies were made.

Spooner[9] reports the results of his observations in a small community in Vermont, in which 65 persons were exposed. 29 of these were inoculated after 17 cases of typhoid fever had been reported; 19 persons refused vaccination; 5 (26.3 per cent.) of the latter developed the disease, while only 1 (3.5 per cent.) of the 29 inoculated persons became ill.

In these reports, it should be observed, the origin of the infection, the means of transmission, the time of disinfecting the transmitting agent, and the relation of the use of vaccine to the period of pollution and use of the transmitting agent have not been noted.

It is the purpose of this paper to contribute to the literature, studies on the use of vaccine during the course of an epidemic in Troy, Bradford County, Pennsylvania. The writer was assigned in charge on October 12, 1912, by Dr. Samuel G. Dixon, Commissioner of Health, by whose permission the results are presented.

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[3] Jour. Roy. Inst. Public Health, London, 1910, vol. xviii.
[4] Russell, Jour. Amer. Med. Assoc., October, 1912, p. 1368.
[5] Loc. cit.
[6] Ibid.
[7] Bull. de l'Acad. de Méd., Paris, December, 1911.
[8] Acad. des. Sci., Paris, June, 1912.
[9] Jour. Amer. Med. Assoc., October, 1912, p. 1359.
[10] Hunt, Jour. Infec. Dis., Chicago, May, 1913.

regularity with which the epidermal processes extend into the adjacent connective tissue, the retention of many of the characteristic contoural and tinctorial qualities of the epithelial elements, the freedom from associated plasma-cell infiltration, and in the vast majority of instances the total absence of malignant tendencies of any kind all point to the correctness of this hypothesis.

On the other hand, in rodent ulcer and allied types of epitheliomas one of the most distinctive and striking features is the apparent freedom of the growth from guidance or restraint of any kind, and the manifest insatiable desire of the constituent cells to tear down and destroy normal structures with which they come in contact.

Although the parasitic nature of malignant growths in man is as yet unproved, the result of the investigations of Erwin F. Smith[9] and others on a strikingly similar disease in plants ("crown gall," due to the bacterium tumefaciens) is encouraging, and it is probable that the discovery and isolation of the causative organism, or organisms, is only a matter of time. Certain states and conditions of the skin undoubtedly predispose to attacks of this kind, and a suitable soil may be inherited as well as acquired. That the changes occasioned by the presence of such an affection as acanthoma adenoides cysticum renders the skin more susceptible to cancerous involvement, however, I consider improbable, and unproved by the evidence now at our disposal.

THE USE OF ANTITYPHOID VACCINE DURING THE COURSE OF AN EPIDEMIC.[1]

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Previous Reports. The use of antityphoid vaccine in military and civil life, particularly in institutions, has been carefully studied. The statistics which have been compiled have presented most prominently the types of local and general reactions observed, the strains of microörganisms used, and, to a much less extent, studies upon agglutinins, bacteriolysins, phagocytosis, and some rather insufficient references to the "negative phase."

However, records of its use as a prophylactic agent during the course of epidemics have been meagre. The earliest record is that by Cullinan, of Dublin (quoted by Wright[2]), who reports inoculations of over 500 persons during an epidemic lasting five months

[9] Moore, Jour. Cutan. Dis., 1912, p. 515.

[1] Read in the Section on Medicine of the College of Physicians of Philadelphia, April 28, 1913.

[2] British Med. Jour., October 26, 1901, p. 1226.

in the Richmond Asylum. Among those inoculated only 1.35 per cent. contracted the disease, all of whom were in the incubation stage of the disease at the time; 14.9 per cent. of 114 uninoculated nurses subsequently developed typhoid fever. Leishman,[3] Wright, and Semple inoculated 100 attendants in the Barming Asylum during the Maidstone epidemic in 1897; none of those vaccinated developed the disease.

It was used extensively in an epidemic in Torrinton,[4] Connecticut, during the summer of 1911, only one case occurring among those vaccinated. Russell[5] mentions its use during an epidemic in Cuba in which 2500 marines were subject to exposure, and again in Cedar Rapids, Iowa, during 1912. Ravenel[6] refers to its use during an epidemic in a small Wisconsin town during the same year. Vincent[7] reported the results obtained by him in Algiers and Morocco. However, as was subsequently pointed out by Metchnikoff,[8] the disease was endemic and not epidemic in the countries in which Vincent's studies were made.

Spooner[9] reports the results of his observations in a small community in Vermont, in which 65 persons were exposed. 29 of these were inoculated after 17 cases of typhoid fever had been reported; 19 persons refused vaccination; 5 (26.3 per cent.) of the latter developed the disease, while only 1 (3.5 per cent.) of the 29 inoculated persons became ill.

In these reports, it should be observed, the origin of the infection, the means of transmission, the time of disinfecting the transmitting agent, and the relation of the use of vaccine to the period of pollution and use of the transmitting agent have not been noted.

It is the purpose of this paper to contribute to the literature, studies on the use of vaccine during the course of an epidemic in Troy, Bradford County, Pennsylvania. The writer was assigned in charge on October 12, 1912, by Dr. Samuel G. Dixon, Commissioner of Health, by whose permission the results are presented.

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aged twenty-four years, had suffered with the disease, from which he had fully recovered, seven months prior to the epidemic. The examination of his feces and urine was negative on the first attempt; on the second examination, made some six weeks after the onset of the epidemic, eight to ten colonies of the Bacillus typhosus were recovered from each cubic centimeter of the diluted feces; these were properly identified, and were subsequently used to study the agglutination of the sera from patients in Troy.

After an unusual period of drought there were two successive and unusual rainfalls, the first one occurring on September 15 and the second during a period of three days, from September 22 to 25 inclusive.

The onsets of the cases occurred at the maximum between eleven and fourteen days after each rainfall. The two curves produced (as determined by dates of onsets) show the fastigia occurring on September 28 and on October 8 to 11. The water was probably continuously polluted from September 15 to October 14, with two periods of maximum pollution occurring immediately subsequent to the rainfalls mentioned. During this period there was a gradual subsidence of the flood waters, so that at the time of disinfection on October 14 the stream was practically at its normal flow. However, there was normally no period of subsidence of the waters used for the municipal supply because the reservoirs were insufficient for storage purposes. These factors are of importance as aiding in the continuance of the infecting agent, and would indicate that while some dilution of the sewage undoubtedly occurred, there was a continuing pollution to which the users of the water were exposed up to the date of disinfection of the supply and of the distributing system. A careful study of all conditions indicates that the incubation periods of the last persons to be infected would extend to about November 3 or 4.

The population of the borough is remarkably stable; while there were certain cases occurring in the townships, they have been included in the census which was carefully made by agents of the State Department of Health. The latter shows that 1343 persons had constantly used the water supply, and these constitute the number who were exposed to infection by typhoid fever from that source. There were 229 cases developed during the entire epidemic, of which but 4 cases were shown to have been secondary.

A mixed vaccine was used, made according to the following formula:

	Syringe 1.	Syringe 2.	Syringe 3.
Bacillus typhosus	500	1000	1,000,000,000
Bacillus paratyphosus A	250	500	500,000,000
Bacillus paratyphosus B	250	500	500,000,000

The organisms used were strains in use in the United States Army Laboratories. The inoculations were given every nine or ten days.

The tabulation of the use of vaccine shows that of the 1343 who were definitely exposed to the infection, 761 (or 56.56 per cent.) persons received inoculations, while 582 (or 43.32 per cent.) persons were not vaccinated. If the total number of persons exposed after deducting 127 persons already sick is used as a basis it would be shown that 62.5 per cent. of those exposed but apparently well at the time of the first inoculation received vaccine.

The first inoculation was given during the week beginning October 14, and while all were not inoculated on the first day, the statistics which are presented are based upon the relation of inoculation to the individual dates of onset.

AGE AND SEX. The study of the age and sex of those inoculated is of some interest; the age periods of the greatest number of persons vaccinated were between fifteen and thirty-five years. However, the predominant age in relation to the morbidity was between five and twenty years. This maximum morbidity occurring at a relatively early age, as contrasted with the age period usually considered most susceptible, was an important factor in the study of the susceptibility of the community as a whole. The wide latitude of susceptibility is shown by the ages of those who were ill, ranging from two and one-half to eighty-four years. It should be noted that this community had always been typhoid-free, and that acute bacillary disease of the intestinal tract was relatively unknown. The ages of those vaccinated conformed to this wide range of susceptibility, ranging from one and one-half to seventy-nine years. 373 (or 49.2 per cent.) presented for vaccination were males, while 388 (or 50.8 per cent.) were females.

RELATION OF TIME OF VACCINATION TO MORBIDITY. Of the 229 cases, 127 developed the disease prior to October 14, the date of first inoculation, and 102 became ill subsequent to that date.

The morbidity in relation to the total number of persons vaccinated and unvaccinated shows:

Number of persons vaccinated	761
Number of persons vaccinated but developing typhoid fever	37 (or 4.86%)
Number of persons not vaccinated	582
Number of persons not vaccinated developing typhoid fever prior to October 14	127
Number of persons not vaccinated and well prior to October 14	455
Number of persons not vaccinated developing the disease subsequent to October 14	65 (or 14.28%)

That is, of all persons who remained well up to and including the date of first inoculation, 4.86 per cent. of the vaccinated and 14.28 per cent. of the unvaccinated developed the disease.

The first inoculation was given on October 14 and the third on November 3. Between these dates, 35 of the 37 onsets in vaccinated persons occurred at varying periods. The inoculation period of those last infected corresponds to the limitations of these same dates, and would extend to November 4.

Morbidity and Mortality of the Vaccinated. The clinical evidence of typhoid fever in the 37 vaccinated persons occurred in 28 persons after the first inoculation, in 7 persons after the second, and in 2 persons after the third inoculation.

The clinical features in the vaccinated are of importance and the analysis of 19 cases shows the following:

1. *The Onset.* This was prolonged in every case; the only evidence of acceleration of onset was the appearance of a recognized temperature (which became continuous) shortly after vaccination in a majority of the cases.

2. *The Type of Temperature.* There was no apparent modification; in all cases it was of continued type, the regular morning remission being noted in the majority, and the defervescence was by lysis.

3. *The Duration of Illness.* The average for all not having a relapse was twenty-eight days, the shortest twenty-one days, the longest thirty-one days.

4. *Relapse.* This occurred in 6 (or 31.5 per cent.); in 1 case the entire period of illness lasted over one hundred days.

5. *The Complications.* Among these may be mentioned the effect on the nervous system, 5 showing marked delirium. Acute nephritis followed in 2 cases; this cannot be accounted for by reason of previous nephritis or any other factor than the present illness. Intestinal hemorrhage occurred in 3 cases, thrombosis and phlebitis in 2 cases, and a lobar pneumonia in 1 case.

6. *The Mortality.* There was one death of those vaccinated, a mortality of 0.27 per cent. This patient, a female, aged seventeen years, received one inoculation on October 18. Date of onset, October 21; the patient was confined to bed November 5; pneumonic dulness, lower lobe, right lung, November 12; severe intestinal hemorrhage November 16; death on November 21. In contrast with this there were 17 deaths among the unvaccinated, a mortality of 8.85 per cent. The case mortality during the entire epidemic was 8.29 per cent.

These results are not in agreement with the statement made by Spooner that the course of the disease is modified by prophylactic inoculations of vaccine. Nor is it possible to compare these statistics with the work of Cullinan or Spooner. The former gives the statistics of an epidemic continuing over a long period of time, the percentage of positive and negative results being for two classes of individuals. Spooner's work, while more useful as a means of comparison, does not state the relation of the use of vaccine to the use of the transmitting agent.

The argument in favor of the use of vaccine under these conditions is found in the relative percentage of morbidity of vaccinated and unvaccinated, strengthened somewhat by the fact that the larger proportion of the population received vaccine and the smaller percentage of those developing typhoid occurred in the vaccinated.

However, it should be noted that the usual morbidity in waterborne epidemics varies from 2 per cent. to 10 per cent. of the population. That portion of the morbidity occurring prior to the first use of vaccine in Troy was 9.45 per cent., and the total morbidity was 17 per cent. of the population. Over 58 per cent. of those becoming ill after October 14 show onsets within five days of that date. Hence the conclusion is formed that some other factors were of importance in determining the value of vaccine in the epidemic—namely, the time, degree, and continuance of pollution and the broader problems of susceptibility of the exposed and virulence of the infecting microörganisms. It would not seem advisable to place too much value upon the use of vaccine until these factors had been considered.

It is obvious that the results obtained would vary with every epidemic reported, as the factors relating to pollution and the continuance vary. However, the underlying principles in the use of vaccine would be the same.

The 2 cases developing typhoid fever after the end of the incubation period for all cases infected are of importance. The first case, E. A., female, aged twenty-seven years, graduate nurse, received the first inoculation on October 25 and the second on November 4. The first subjective evidences of the disease were noted on November 5. This was followed by the development of temperature which ran a normal course, subsiding by lysis to normal on November 25. The recrudescence appeared on December 1 with a temperature course lasting for two weeks. The patient gave the usual history and clinical picture of typhoid fever. It is altogether probable that this patient was infected just prior to the disinfection of the water supply; she may have been a secondary case, although there are reasons to exclude the latter factor.

The second case, H. B., a male, aged twenty-three years, is of greater interest. He received his first inoculation on October 16, the second on October 26, and the third on November 10. The onset of temperature occurred eight days later, November 18, and ran the usual typhoidal course, returning to normal by lysis on December 4. During the course of the disease he suffered slight intestinal hemorrhage, but there were no other evidences of complications, and recovery was uninterrupted and complete.

Even if the incubation period had been the maximum of thirty days noted in a small percentage of cases, his onset would date four or five days subsequent to the abatement of the source. Regardless as to what time and where he acquired his infection, the development of the disease in its typical form, occurring eight days after the third inoculation, would suggest that antibodies had not been created in sufficient amounts to give protection.

Determinative Usage. The value of an antivaccine of this type during the course of an epidemic seems to be determined by

the time of its use in relation to many factors, of which the principal ones are as follows:

1. *The Abruptness of Pollution of the Transmitting Agent.* With the common agents—namely, water, milk, and ice-cream—there is the widest latitude for a long-continued or an abrupt pollution to occur. It is during epidemics in which these are the agents that the use of a vaccine must be most carefully considered. Its use to prevent infection through all other agencies is apparently as valuable as its use in military and institutional experience seems to indicate. However, in an abrupt and unrecognized pollution the actual benefits are questionable, and it is far from being proved that it is wise under such conditions to use it until the incubation period of those early infected has ended or until careful exclusion by blood culture indicates that the applicant is not already a potential patient.

2. *The Degree of Pollution.* It is obvious that a small amount of sewage introduced into a large volume of water would lessen the possibility of infecting the users of that supply. If there is a mass pollution of the supply the epidemic tends to assume the explosive character so frequently recorded in water-borne epidemics. Other factors influence the results when the agent is other than water, but the principle is constant. When mass pollution occurs the immediate results are similar to those when the pollution is abrupt, but less concentrated, and the use of a vaccine during the early portion of the epidemic must depend on a careful analysis of each applicant, not only as to his immediate physical condition, but also as to his use of the suspected or known source of infection.

3. *The Susceptibility of those Exposed.* Individual susceptibility is too large a subject to discuss within the limitations or purposes of this article. However, when a community has for a long period used a water supply which is constantly carrying sewage, the individuals seem to develop what has been called by Adami[11] an "accustomance" to long-continued and often repeated minimal doses of toxins of the infecting microörganisms. This resistance is not apparent but real. One Pennsylvania town using a known sewage-polluted stream has suffered with endemic bacillary infections for many years. During the past ten years upward of 90 per cent. of those developing typhoid fever have been children. In Troy the high-case morbidity (17 per cent.) and the community history suggest the importance of a community resistance, and it would seem that the results of the use of vaccine would be modified by this acquired resistance.

4. *The Virulence of the Specific Strain causing the Epidemic.* This has been shown to be of importance in many epidemics occurring in Pennsylvania. Two types serve to illustrate its importance.

[11] Principles of Pathology.

The mortality as recorded in an epidemic in Indiana County was 14.8 per cent.; the residents were, for the most part, foreign-born and accustomed to the use of promiscuous water supplies. The organisms were transmitted by means of a spring-water supply from cases suffering with a virulent form of the disease. In the Troy epidemic the strain of the bacillus causing the epidemic was recovered from a carrier and the mortality was 8.29 per cent. These two epidemics were water-borne and the abruptness of the onsets and the degree of pollution were similar. The difference in mortality can be explained only by the difference in virulence of the specific strain of the microörganism, and to a less degree the susceptibility of those who were infected.

5. *The Time of Use of the Vaccine in Relation to the Use of the Source of Infection.* This is obviously of the greatest importance. If the infection of patients occurs as the result of a high degree of pollution which has been quickly established it is probable that vaccine prophylaxis will be of no value. However, in epidemics in which there is a low degree of pollution, even if the pollution occurs abruptly, the insusceptibility of many of those exposed will prolong the incubation period; in others, the infection may occur late during the course of the epidemic, and, in addition, there are unexplained cases occurring over a long period after the epidemic has subsided. After exercising care to analyze each applicant's case the prophylactic use of vaccine may seem advisable in these latter cases.

6. *The Number of Bacteria or the Amount of Vaccine Used.* In no other condition does the number of microörganisms or the amount of vaccine assume the same importance as in persons who are in the prodromal stage of the disease. It is, at least theoretically, unwise to give maximum prophylactic inoculations to such persons. It is desirable, during an epidemic (if the patient is not in the prodromal stage of the disease), to establish immunity as quickly as possible and with the least number of inoculations. This implies an increase in the dosage, which is opposed to the underlying principles of vaccine immunization. The production of active immunity by the formation of specific antibodies cannot be done in a hurry. The use of larger doses than are used at present has already been shown to be followed by undesirable phenomena in healthy persons. Hence for two very good reasons it would not seem advisable to give maximum doses to a healthy person and much less to one who is a potential case of typhoid fever.

7. *The Possibility of the Existence of a "Negative Phase,"* which was first discussed by Wright,[12] has not been absolutely eliminated from consideration, although Leishman states that the dangers

[12] British Med. Jour., January 30, 1897.

are more theoretical than real. Russell[13] quotes Cullinan, Leishman, and the "consensus of opinion of the 1907 International Congress of Hygiene" to prove its unimportance. Leishman[14] also states that the most important evidence must come from actual practice rather than from laboratory experiment. The "actual practice" in Troy indicates the inadvisability of adding large doses of toxins to patients whose poise between susceptibility and resistance already hangs in the balance. If an interval of decreased resistance does exist between inoculation and the formation of antibodies it is of the greatest importance in those who have been exposed to infection. The first opinion entertained after studying the Troy cases was in agreement with Spooner,[15] who suggests "an acceleration of onset" in the infected vaccinated case. A closer analysis fails to confirm his opinion; the prolonged incubation period in all cases, the delayed onset until many days after the second inoculation in 4 cases and until seven days after the third inoculation in one case, outweighs the appearance of the occurrence of clinical evidences of disease in 11 cases coincident with the first inoculation. On the other hand, the negative phase is believed not to last more than "several days" (Wright) unless it is prolonged by large doses. While no positive statements as based on the Troy cases can be made it is to be inferred that resistance to the infecting bacilli had been temporarily lessened.

8. *The Types of Vaccine* so far used during epidemics have been limited to strains of the Bacillus typhosus only. In Pennsylvania epidemic experience has sufficiently justified the very certain belief that the paratyphoid fevers and, to a certain extent, infections by organisms of the Gaertner type are endemic and may be almost as great a menace as are infections by the Bacillus typhosus.

The studies of atypical cases in Coatesville, Iselin, and elsewhere indicate the prevalence of mixed infections, particularly when water-borne. For this reason vaccines which include other forms would seem to be of greater value than a vaccine including only the Bacillus typhosus strains.

Lyons[16] studied paratyphoid vaccine therapy after observing that an attack of typhoid fever and the use of antityphoid vaccine failed to protect against paratyphoid fever. Kabeshima[17] inoculated 300 men with mixed vaccine containing typhoid and paratyphoid strains, because the hospital admissions for three years showed paratyphoid fever was eight times in excess of typhoid fever. The results of his observations were apparently highly satisfactory.

Riesman,[18] in a recent report to the College of Physicians of

[13] Boston Med. and Surg. Jour., January 5, 1911.
[14] Loc. cit.
[15] Loc. cit.
[16] New Orleans Med. and Surg. Jour., November, 1911.
[17] Bull. Naval Med. Assoc. of Japan, May, 1912.
[18] Trans. Coll. of Phys., Philadelphia, 1913.

Philadelphia, reviewed cases of paratyphoid fever under the suggested title of "entericoid fever," and emphasized the value of mixed vaccine. The absence of a co-immunity between microorganisms of the typho-colon series was shown in his cases, as all had had typhoid fever within three and one-half to twelve years.

A mixed vaccine of this type in epidemic work has not previously been reported. So far as the prevalence in Pennsylvania is concerned the value of a mixed vaccine in routine immunization is emphasized. In epidemic use it would be limited to those who had not been exposed to the original source of infection.

In a report[19] of this epidemic it was stated that "the use of antityphoid vaccine was an important factor in preventing a number of cases." By this was meant the prevention of secondary cases and the cases which practically always occur in the aftermath of a water-borne epidemic. The latter form an interesting study, since they occur even when engineering interference is prompt and apparently efficient. It may be they are infected from carriers (formed during the epidemic), and should be included among the secondary cases.

The pertinent conclusions from the studies made in this one epidemic indicate the little value antityphoid vaccine has in limiting the number of cases and in modifying the process in the individual case. It would seem since antityphoid serum confers relatively a more immediate and fairly strong immunity that a serum would be of some advantage during such an epidemic. The use of vaccine should be limited to those not already infected, that is, to prevent secondary cases. To this end the individual history and diagnosis by culture would determine its use.

I desire to express my great appreciation to the physicians in Troy for the opportunity to study their cases, and to these same physicians and those from Canton and Towanda who assisted in the administration of vaccine.

A STUDY OF CASES OF ACTINOMYCOSIS.

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(From the Pathological Laboratories of the Royal Victoria Hospital, Montreal, under the direction of O. C. Gruner, M.D.)

A study of the clinical histories and subsequent course of the cases of actinomycosis in the Royal Victoria Hospital during the past twelve years has revealed many features of great interest. The fact that the disease is not uncommon in rural communities,

[19] Hunt, loc. cit.

and that it is frequently mistaken for tuberculosis, or even malignant disease, even by the most astute diagnosticians, renders it advisable to discuss the character of the disease, since an early diagnosis is important if suitable lines of treatment are to be adopted.

The history of the subject may be briefly summarized as follows:

A disease occurring in cattle, in which the chief symptom was swelling of the jaw, was described by Le Blanc in 1826. A similar condition was mentioned by Professor Dick in 1833, and he surmised that the same disease occurred in man. In 1845, Langenbeck described a case of vertebral caries in a young man, the pus from which contained numerous sulphur-like granules. In 1850, Devain described a tumor of the jaw in an ox, the pus from which contained yellow granules similar to those described by Langenbeck. He stated that, microscopically, the characters were neither those of tubercle nor of malignant disease. In 1858, a case in which the thorax was affected was described by Lebert, and similar cases were reported about the same time by Laboulene, Robin and others. A disease known as *mal di rospo* in Italy, in which the prominent symptom was a tumor of the jaw, was studied by Rivolta in 1863, and five years later he discovered rod-shaped bodies in the pus. He was unable to inoculate successfully, but later established the identity of the disease in the horse, dog, and most of the domestic animals.

While isolated cases were discovered after this date, it was not established until 1877 that the peculiar rod-like bodies found in the jaw in tumors of oxen were the cause of the disease.

Bollinger, and his botanical colleague Hartz, of Munich, recognized the parasitic nature of the bodies and gave the name "ray fungus" to them, owing to their radiate appearance. In 1878, Israel described two cases of a new form of mycosis in man, and isolated the fungus from multiple abscesses. The following year Ponfick found the same fungus in a prevertebral abscess, and suggested the identity of the disease in man and in animals. Johne successfully inoculated an ox with the yellow granules. The latter were first studied by Perrocito in 1875, who noted their occurrence in what was considered osteosarcoma of the jaw. In England, Auckland (1899) was the first to meet with a case in man, the liver being the part affected. The disease was studied in animals in the United States by Bellafield, of Chicago, in 1883, and Murphy described similar cases in the human subject shortly afterward. The first case recognized in the human subject in Canada was diagnosticated in the Royal Victoria Hospital, Montreal, in 1900, in a case of persistent lumbar sinus of obscure origin under the care of the late Dr. James Bell, at whose instigation Dr. A. G. Nichols was able to demonstrate the fungus.

Geographical Distribution of the Disease. The environs of Berlin, Germany; the salt marshes of Russia; Italy; Austria; part of England; North America.

In our own cases the remarkable fact was noted that with the exception of three or four cases they all came from locations within a hundred miles of Montreal. One small strip along the St. Lawrence River furnished a large number of our cases, and the other locality was south of Montreal and in the eastern townships. In the city itself several cases have occurred, all in the north or east of the city. The reason lies in the fact that there is a greater opportunity for infection in these localities.

Season. It is a remarkable fact that nearly all our jaw cases come to us between September and January (see List of Cases), while the abdominal and pulmonary cases are usually admitted late in the spring, having, however, complained of symptoms for a considerable period (see List of Cases). This is natural when one considers the mode of infection from grain. The lesion on jaws makes itself apparent earlier, while the deeper abdominal conditions take longer to manifest themselves. In cattle the disease is most common in dry-feeding periods.

Sex. Males are infected much more frequently than females. In our series of 37 cases only 9 were females.

Appendix	1 female out of 13 cases.
Left groin	2 females out of 3 cases.
Cervicofacial	6 females out of 19 cases.
Others	0 females out of 2 cases.

Females usually take better care of their teeth, and are less liable to chew straws, or to be brought into contact with infection.

Age. The youngest case was aged ten years, the oldest, fifty-four years. Most frequently the age was between twenty-five and thirty-five years. The disease is rare in children.

Occupation. Males: farmers, 19; laborers, 5; steam-fitters, 2; clerks, 2; superintendent of car works, 1; electric engineer, 1; bricklayer, 1; grain merchant, 1; millwright, 1; cheesemaker, 1; merchant (country), 1; lawyer, 1.

Race. No race seems immune. All of our cases have occurred among whites, but since negroes are not numerous in the affected region, our own statistics afford us no data under this heading.

Methods of Infection. The organism is widely distributed in nature and is easily isolated from certain grasses. Direct contagion is denied by many observers (Leith). On the other hand there have been cases reported where men have contracted it from animals infected with the disease (Barazac mentions two cases). Finally, at the Royal Victoria Hospital, one of the earliest cases occurred in a nurse who had been attending a case of actinomycosis. The proof for direct infection is not very convincing, but the above case and other suspicious ones render it likely that it does occur at times if the conditions for infection are favorable. There is not much evidence in favor of direct infection from animal

to animal, and there is considerable evidence against it, with one interesting example. Salmon put twenty-two healthy cattle with infected ones for a period of four months and none developed the disease.

Infection by Milk. The mammæ of cattle are rarely infected by the disease. If the disease originated from milk we would expect to see it more frequently in babies, in whom, however, it is exceedingly rare.

Infection by Food. Here also several factors exist which do not permit the probability of infection: (1) The parts affected by the disease are not used for food, and (2) the ordinary process of cooking destroys the organism.

Infection from Plants. There are numerous examples and experiments which go to prove that direct infection from plants can take place. Johne found a husk covered with fungus in the tonsil of a pig, and several French cases are reported where injuries have occurred while handling grain, followed a few days later by the appearance of the disease.

Conditions Necessary to Infection. Johne, in 1888, fed animals on food mixed with cultures of the organism, but in no case did the disease develop. It is to be noted that in all our jaw cases of actinomycosis we have never had abdominal infection. The favorite sites of intestinal actinomycosis are the cecum, appendix, and rectum; in the pulmonary cases it is most frequently right-sided, and attacks the base rather than the apex of the lung, in contrast to its kin tuberculosis.

It has been proved by Johne and others that cattle fed on virulent cultures will not acquire the disease. It seems that the carrier of the microbe must be able to penetrate the surface (chewing straw), or there must be some abrasion present, for example, soft spongy gums around a carious tooth. The proof of this in all our jaw cases lay in the fact that the teeth on the affected side were in bad condition, and that the disease affected either the upper or lower jaw according to the situation of bad teeth. The fact that the presence of an ulcerated surface is needed to permit the entrance of the organism into tissues explains why the disease is more common in the appendix and rectum. According to statistics, there are inflammatory changes and small ulcers, etc., in the appendix in 75 per cent. of healthy adults. Again, in this region the process of movement is retarded; the fecal mass is becoming more solid and remains longer in the area. Solid particles themselves may cause abrasions which permit the entrance of the organism. For the same reasons the rectum is more likely to show superficial ulceration. The reason that ulcer of the stomach is not more often affected is because the acid of the stomach prevents the growth of the organism. In fact, it is rare to see secondary infection of any chronic ulcer by actinomycosis. It seems to

flourish best in acute lesions. It has been reported as occurring in typhoid ulceration.

Infection by Inhalation of Dust While Threshing. Pulmonary infection by inhalation may occur, but this is rare. Israel pointed out that it was impossible without some associated injury to the tissue of the lung. In one case the disease started around a portion of an aspirated tooth, and in another a barley beard was the originator of the focus. Again, in all our pulmonary cases there had been abdominal symptoms previously. In one case the appendix abscess was opened, drained, and healed, and one year later an abscess developed over the thoracic wall, which was opened and drained. The appendix condition had apparently healed up, the mass disappeared, and all that remained was the scar. Again, the fact that it most frequently involves the lower lobe of the right lung is also strong evidence in favor of infection via the appendix—that is, ascending infection. It is not necessary to have a marked appendix lesion to have pulmonary symptoms, but if the appendix were examined in every case of pulmonary actinomycosis we should most likely find some evidence that the organism had gained an entrance to the circulation from that site. In left-sided cases the seat of the original trouble is probably the rectum. In two cases the original trouble was in the groin, in another the abdominal wall. The organism spreads, as stated above, by blood, but occasionally by lymphatics, as in a case of primary rectal infection reported by Bevan, in which the inguinal glands were involved. The fact that injury is necessary for the entrance of the organism is further emphasized by the fact that cattle living on salt marshes which are periodically covered by the sea are more susceptible, the jaw being injured by sand-shells, etc.

Bostrom observed beards of grain in 11 cases. Frequently there is the history that the patient used straws as toothpicks.

An example following an injury to the finger is given by Suchard.[1] The wound was caused by a spike of corn penetrating the index finger. In eight days a small pustule appeared.

Ziemann, in 1883, reports one case of infection occurring through the vagina.

Incubation Period. This varies from a few days, as in our jaw cases, to weeks and months in abdominal and pulmonary cases.

Local Tissue Changes. The organism having found lodgement in the tissues sets up hyaline degeneration in the tissues immediately around. In stained specimens there is a central bright pink homogenous mass inclosed in a more or less dense collection of round cells (mononuclears). Further away from the lesions we find numerous large spindle cells; and a few giant cells appear, par-

[1] La Presse Médicale, August 15, 1903.

ticularly in the outer zone of infection. There is a new form of connective tissue about the foci of infection, which in cattle is prone to undergo calcification, while in man this change is rare. In the interstices of the new-formed tissue colonies of the streptothrix are found with their attendant zone of inflammation as described above. When there is an excessive production of connective tissue the cases partake of the nature of newgrowth. An overgrowth of streptothrix in one of these interstices leads to break-down and formation of sinuses, or of an abscess. The disease spreads by contiguity and along the blood stream, rarely by lymph channels.

The pus from the cavities is small in quantity and has a peculiar earthy odor, is usually blood-stained, and contains the characteristic sulphur-yellow granules, which in cattle possess a very gritty feel, and are found under the microscope to be colonies of the organism. The central part of a colony consists of a mass of filaments (mycelium) which form a dense felted network. At the periphery there are large pear-like forms which have received the name of clubs; coccus-like forms (probably cross-views of filaments) are also present. The mycelium is made of long thin threads, which are frequently wavy, like spirochetes. They consist of a shred of protoplasm, which shows much fragmentation in old cultures, and at their tip is dichotomous branching. The fragmentation gives the filaments the appearance of chains of streptococci of varying length. They are positive to Gram.

The Clubs. These appear to be the swollen terminal extremities of the filaments. They are more frequently met with in cattle than in man, and are more abundant in chronic cases. They have a pale hyaline appearance, are pear-shaped, and negative to Gram. They are probably degenerative forms, and result from the action of the body juices on the filaments. They are best seen with the low power after crushing the material with 10 per cent. potash under a cover-slip. The central granular mass with arrangements of filaments or clubs around it is then characteristic.

The organism grows with so much difficulty on all ordinary media that cultural methods are of no practical value to the clinician. Liebman was able to grow the streptothrix on plants, and he also showed that it became attenuated by passing through the animal body (unlike most organisms), and regained its virulence after being grown on plants. This probably explains why infection from one animal to another is rare.

Site of Disease. In domestic animals it is most frequently met with in the jaw, except in Russia, where it is the skin which is most frequently affected. As regards man, the statistics given by Rurähh of 1094 European cases are: Head and neck, 56 per cent.; digestive tract, 20 per cent.; pulmonary, 15 per cent.; skin, 2 per cent.

Our statistics of 37 cases record the following: Cervicofacial, 19; appendix, cecum, and abdominal wall, 13; left groin, 3; left groin, lumbar region, 1; skin, 1.

Clinical Features of the Histories of Our Cases. The clinical history of a disease so varied in its manifestations presents some difficulties in description. Here again it resembles tuberculosis, but is best studied by considering in turn the various regions of the body affected. I will here confine myself to the regions exemplified by our own cases, that is, the jaw, cecum, appendix, and thorax, by giving a short account of actual cases.

1. *Appendix Cases.* In all we have had 13 cases diagnosticated actinomycosis of appendix and abdominal wall, 2 of which are doubtful, leaving 11 undoubted cases. Unfortunately the majority of the cases that ended fatally were sent home before death, and with the exception of our first case and Case 10 (see List of Cases), no autopsy, or only a very superficial one, was made. The fact brought out by the cases is the high mortality. We can report only 2 cures. The diagnosis was rarely made before operation, not even until a fistula formed which occurred in 9 cases out of 11 (Cases 2, 3, 4, 5, 8, 9, 10, 11, 13), from the pus of which the organism was isolated. Lung and liver complications occurred in 8 cases (1, 2, 5, 6, 8, 10, 12, 13). Cases 5 and 13 show the liability of the disease to completely heal at the site of inoculation and reappear in other localities far removed.

Clinical Features of Appendix and Abdominal Wall Cases. Males are more affected than females, 12 to 1. The patients usually come to the hospital between January and May, differing in this respect from jaw and cheek cases, which usually come to the hospital between September and January.

The initial symptoms are, as a rule, like those of acute appendicitis, differing from the ordinary form in that the patient never completely recovers after the attack. Vomiting is not so frequently present with the attacks, while diarrhea is much more constant. A peculiar hard mass soon forms, and flexion of the psoas muscle is often early and marked. In fact, the difficulty in straightening the leg is frequently noticed before the mass is discovered. As the disease progresses jaundice not infrequently develops, and later on loin and subphrenic abscesses appear, with final involvement of the lungs. If operated upon the character of the muscular infiltration with small amounts of pus may point to the diagnosis, but even then the surgeon may fail to appreciate the condition until the later developments of fistulæ and sinuses which will not close, but continue to discharge pus-containing yellow granules, leads for the first time to the discovery of the organism.

2. *The cervicofacial cases* were 19 in number. The after-history was particularly difficult to trace, but some of these patients would probably have returned to the hospital for treatment if they had

had a recurrence. Cases 1, 2, 5, 15 could not be traced. Cases 13 and 14 showed no improvement. In Case No. 4 the organism was doubtful. Case No. 9 is particularly interesting from the chronicity; began in 1904, and from then until October, 1911, had 100 operations, consisting of opening, curetting, etc.; died, June, 1912, from nephritis, after having nine months' freedom from disease. The cause of death was recorded as due to excessive chloroform, ether, and perhaps potassium iodide, which he took for long periods (60 gr., t. i. d.).

Females were affected in 6 cases; the remainder were males. In all cases decayed teeth were present. Patients began to have trouble in the early fall, coming to the hospital between September and January.

The jaw and cheek cases have certain points in their history and clinical course which are almost characteristic: (1) There is usually a history of bad teeth, the appearance of a gum-boil near the decayed tooth which will not heal; (2) the tooth being extracted, the abscess is better for a while, but reopens, until finally the process involves the cheek, and as it comes near the surface the skin over it has a characteristic color—a dark, glossy, purplish red. The chronicity of the affection is well exemplified by a case that came first in 1902 (Case No. 9 cervicofacial series) and has been coming at intervals every year since.

3. *Clinical Features of the Groin Cases.* The cases occurred in 2 females and 1 male. The females both recovered and we were unable to trace the after-history of the third case. So far as our limited experience reaches, it is relatively good as regards prognosis. There is nothing of much interest to note in the clinical symptoms other than the fact that in all our cases abdominal symptoms were present, and a doctor was only consulted when a mass was recognized. In Case 1 urinary symptoms were complained of, but operation revealed no connection between bladder and abscess cavity. Unfortunately in none of these cases was a rectal examination made, and there was no mention of hemorrhoids or fissure in the case reports. In any event it is probable that the seat of infection was from a fissure or ulcer in the anus or rectum, and to explain its occurrence in the left groin, lymphatic extension from the anus to the groin is the only intelligible way of explaining it. This method of extension is rare, but such cases have been reported (Bevan).

4. *The pulmonary lesions* as stated above may begin from an air infection, provided there is the necessary injury, but in far the largest number of cases the primary lesion is in the appendix, although the disease may be entirely manifested in the lungs. When occurring in the lungs we have to differentiate it from tuberculosis. The points are that in actinomycosis there are usually some transitory gastro-intestinal symptoms of rather acute char-

acter. The base rather than the apex is affected. Hemoptysis is the exception. Jaundice is frequently present. The organism is found in sputum. Infection travels from below up, not *vice versa*.

5. *Our one skin* case began as small vesicles, which coalesced to form a chronic ulcer with ragged edges and sloughy base. The organism was never isolated. Excision. Patient cured.

PROGNOSIS. The prognosis varies with the situation and extent of the lesion and the initial virulence. A large lesion and the relation to important structures are bad factors. Jiron gives the following statistics of mortality: Face and neck, 11 per cent.; thorax, 83 per cent.; abdominal, 71 per cent.; cerebral, 100 per cent.

Our cases show better results as regards face and neck, as mortality is almost *nil*, but our thoracic and abdominal cases have been almost invariably fatal, over 95 per cent. having died.

TREATMENT. When possible, as in the case of the cheek, total excision is best; in other places the routine is: Opening, followed by curetting, washing the cavity with weak solution of iodine, packing with iodoform gauze, and giving large doses of potassium iodide. The iodide does not act on the organism itself, but seems to have some effect on the tissues, which enables them to overcome the disease (Prutz). When iodides have failed, copper sulphate and various other remedies, including *x*-rays, have been used, but nothing so far replaces the iodides. Our experience here is that *x*-rays are distinctly harmful, causing a spread of the disease in both actino- and blastomycosis.

SUMMARY. 1. Actinomycosis is a more common affection than is generally believed, especially in rural communities.

2. It is frequently mistaken for tuberculosis or newgrowth.

3. There are certain characteristics about the cases from each locality which lead to suspicion of the nature of the disease.

4. The usual situations are the jaw, cheek, appendix, and cecum, with thoracic involvement.

5. Infection cannot occur without a lesion in the skin or mucous membrane.

6. Jaw cases are more frequent in the fall of the year, abdominal and thoracic cases in winter and spring.

7. The onset is often acute.

8. Abdominal actinomycosis shows peculiar liability to fistula formation and tendency to heal at the site of the initial lesion, appearing elsewhere.

9. Abdominal and thoracic forms show high mortality. In skin and jaw cases the prognosis is satisfactory.

10. Diagnosis of primary pulmonary actinomycosis, even in the absence of abdominal symptoms, must remain doubtful without careful postmortem examination.

11. In all our pulmonary forms there has been a previous history of abdominal symptoms.

12. Excision is the best method of treatment where possible. Otherwise, free incision, curetting, washing with weak iodine solution, packing with iodoform gauze, associated with large doses of potassium iodide internally, should be adopted.

13. The relation between cattle and human actinomycosis is closer than that between human and bovine tuberculosis.

In conclusion, I desire to thank Dr. O. C. Gruner, chief of the pathological department of the Royal Victoria Hospital, for his assistance in the preparation of this paper, particularly in the postmortem work.

APPENDIX SERIES.

CASE 1.—Farmer, male, aged twenty-two years, residing, at Ontario. Seat of disease, liver. Duration of symptoms before admission, three months. Admitted, March, 1900.

Chief Features of Illness. Began with loss of appetite; feeling of malaise; crampy pain in abdomen; two months ago slight cough developed, with some expectoration. Temperature at night 103°. One week ago sudden onset of severe coughing, with profuse greenish-yellow expectoration. This was followed by slight improvement. Patient had had what was diagnosticated as pleurisy twelve years previously.

Treatment. Exploratory puncture revealed only blood-stained serum. Tenth rib resected. Lung adherent to diaphragm. Little pus found. Drainage.

Result. Died.

Remarks. Clinical diagnosis made at operation never confirmed by isolating organism until autopsy was made. Notes of autopsy: First case of actinomycosis positively demonstrated in Canada; was diagnosticated primary actinomycosis of the liver because the largest mass was there and because no primary focus was found elsewhere. The appendix was found in the pelvis covered with adhesions. Microscopic diagnosis was chronic appendicitis. This was the probable source of infection, but was not considered so at the time of autopsy.

CASE 2.—Farmer, male, aged fifty-four years, residing at Province of Quebec. Seat of disease, retroperitoneal glands. Duration of symptoms before admission, two months. Admitted, April, 1900.

Chief Features of Illness. Sudden onset of pain in abdomen, with diarrhea. No nausea or vomiting. Attack lasted four days. In short period of time had several similar attacks. Thigh became flexed on abdomen. Complained of pain in sacral region and down thigh. On examination, tender mass was felt in lower right quadrant.

Treatment. Abdomen opened as for appendix. Considerable necrotic tissue in region of appendix. Drained.

Result. Died at home. No autopsy.

Remarks. Several operations performed to close sinuses without avail. Appendix never located.

CASE 3.—Farmer, male, aged forty-five years, residing at Ontario. Seat of disease, appendix and cecum. Duration of symptoms before admission, one month. Admitted, November, 1900.

Chief Features of Illness. Pain in right ileocecal region, coming on suddenly without apparent cause. Shortly afterward, difficulty in walking. Thigh flexed. Appearance of mass. Lost thirty pounds in weight.

Treatment. Incision parallel to crest of ilium, 1½ cm. above. Muscles present peculiar cartilaginous appearance. Little bleeding. Small amount of pus. Drainage. Potassium iodide.

Result. Died at home.

Remarks. Appendix could not be located. No lung complications.

CASE 4.—Farmer, male, aged thirty-eight years, residing at Province of Quebec. Seat of disease, appendix and cecum. Duration of symptoms before admission, three months. Admitted, August, 1902.

Chief Features of Illness. Sudden onset of pain in right iliac region. No vomiting. One week later appearance of mass in right iliac region and flexion of thigh. All symptoms increased on extension of leg. Remained in bed for three weeks, then got up. Lump remained, and gradually increased. Symptoms subsided. Has been moving about. Leukocytes, 6400. Lately complains of pain down front of thigh. Examination reveals a tender hard mass in lower right quadrant.

Treatment. Appendix lying behind cecum was broken off and removed. Two small seeds found in appendix. Drainage. Fistula formed.

Result. Died at home.

Remarks. Several operations performed to close fistula. Seeds in this case were probably conveyors of infection. Organism never isolated from seeds. Appendix showed small ulcerations of mucosa. Walls thickened and friable. Was diagnosticated acute appendicitis on chronic interstitial. The condition was not suspected until fistula formed, and then the organism was found in the pus.

CASE 5.—Farmer, male, aged thirty-six years, residing at Ontario. Seat of disease, appendix. Duration of symptoms before admission, two months. Admitted, April, 1903.

Chief Features of Illness. Sudden attack of sharp abdominal pain lasting several hours, replaced by dull ache in right lower quadrant. No vomiting or diarrhea. Leukocytes, 16,000. Flexion

of thigh, and mass palpable. Some loss of weight. Slight jaundice. Readmitted in August. Pain in right shoulder and in upper right quadrant. Jaundiced at intervals. Liver dulness increased. Evidence of fluid in right base. Some cough and expectoration.

Treatment. Appendix incision. Abdominal walls infiltrated. Large abscess opened into. Loin drain established. Sinus remained. Discharged from the hospital in June.

Result. Died at home.

Remarks. Peritoneal cavity apparently normal. The old lesions had apparently cleaned up, the disease existing only in tissue of abdominal wall.

CASE 6.—Schoolboy, aged thirteen years, residing at Province of Quebec. Seat of disease, appendix, liver, and pleura. Duration of symptoms before admission, three months. Admitted, November, 1906.

Chief Features of Illness. Acute attack of appendicitis. No vomiting. Remained in bed one week, but never completely recovered. Several similar attacks. Patient walked with slight limp. Right pleural cavity contained fluid. Cough and expectoration.

Treatment. Ninth, tenth, and eleventh ribs resected. Only a small amount of blood-stained fluid. Discharged from the hospital in a critical condition.

Result. Died.

Remarks. No abdominal operation or autopsy. This patient was sent to the hospital for the lung condition. A diagnosis of empyema was made. The abdominal condition was overlooked; at the hospital the relation between the two conditions was noted.

CASE 7.—Farmer, male, aged fifty-one years, residing at Province of Quebec. Seat of disease, appendix. Duration of symptoms before admission, one month. Admitted, September, 1907.

Chief Features of Illness. Sudden onset of abdominal pain, with chilliness. No vomiting. Next day seen by the doctor, who discovered hard mass in right iliac fossa. Loss of weight had been considerable.

Treatment. Refused operation.

Result. Not known.

Remarks. Could not find out about patient.

CASE 8.—Millwright, male, aged forty-two years, residing at Montreal. Seat of disease, appendix and lung. Duration of symptoms before admission, five months. Admitted, February, 1912.

Chief Features of Illness. Began with an attack described as inflammation of bowels, with some vomiting. Remained in bed three days and about house five weeks. Never became completely well. Three weeks later developed pain in thorax along costal margin. Doctor diagnosticated pleurisy. One night sudden onset

of severe coughing, with considerable expectoration of greenish color, foul odor. No hematemesis. Quantity of expectoration gradually diminished. Few weeks before admission appearance of abscess in right loin. Examination of thorax shows increase of liver dulness, with diminished breath sounds and resonance over whole of right side as high as third rib. *X*-rays showed the diaphragm unusually high on right side and completely fixed.

Treatment. Abscess in loin opened and drained, packed with iodoform gauze. Potassium iodide by mouth. Sinus led up over the ribs toward thorax. Washing with iodine. Small abscess opened over the tenth rib on right side in anterior axillary line. Several attempts made to close lumbar sinuses by curetting, but finally fecal fistula developed.

Result. Died at home.

Remarks. No autopsy.

CASE 9.—Housewife, female, residing at Ontario. Seat of disease, appendix. Duration of symptoms before admission, one year. Admitted, January.

Chief Features of Illness. Complained of headache, distress in right groin. Small abscess pointed to right iliac region. Opened in June by doctor outside, and appendix removed. Pus evacuated. Abscess healed for short time, reappeared since. There remained a discharging sinus on entrance to the hospital.

Treatment. Abdomen when opened contained straw-colored fluid. The general peritoneal cavity was free. Small sinus leading down to appendix was curetted. Abdomen closed. Sinus packed with gauze. Potassium iodide internally.

Result. Cured.

Remarks. At first thought origin was from genitalia. Diagnosis not made until fistula developed.

CASE 10.—Clerk, male, aged eighteen years, residing at Vermont. Seat of disease, appendix and abdominal wall. Duration of symptoms before admission, six months. Admitted, April, 1912.

Chief Features of Illness. Onset of pain in epigastrium, with slight nausea and vomiting. Patient remained in bed five weeks, the pain gradually subsiding, but never completely disappearing, and later felt entirely in right lower quadrant. Fever during this time continuous. Diagnosis of typhoid made by doctor. Condition of patient improved, and was allowed up. Shortly after, swelling appeared in the right lower quadrant. Leg became flexed and pains became severe, extending down right leg. No vomiting or diarrhea. Patient operated upon on admission to the hospital. Incision in appendix region. Muscle much infiltrated. Appendix never found. Wound packed with gauze. Patient discharged, with sinus still persisting (May). Readmitted in June. Improved for short time after leaving the hospital, then gradually became worse. Ten days before second admission to

the hospital, sudden chill followed by profuse sweats, high temperature, cough and expectoration. Second operation, June 11, over gall-bladder region. Liver enlarged, covered with lymph over region of falciform ligament.

Result. Died June 17, during attack of severe dyspnea.

Autopsy. Thorax: Pleural cavities filled with clear fluid. No adhesions. Lungs emphysematous. Cut surface edematous and consolidated throughout; very friable. Scattered throughout and particularly numerous beneath the pleura, were numerous firm, gray nodules about the size of a split pea, many of them broken down in the centre, forming small cavities containing pus.

Peritoneal cavity: Free from fluid. Appendix short, thick, firm, showing numerous adhesions about. Mesenteric and lumbar glands enlarged. Mesentery normal in appearance, showing no evidence of thrombosis. Appendix measured 4.5 cm.; small, conical in shape; serosa roughened and granular from old adhesions; tip obliterated. A section was composed entirely of a layer of dense fibrous tissue; at the proximal extremity the lumen was increased in size; cavity filled with pus of yellowish color, containing one or two sulphur-like granules, in which rather atypical actinomyces were discovered. The clumps were small and much fragmented. In the walls of the appendix itself no actinomyces were demonstrated. In a small abscess at the lower end of the cecum a few thread-like forms were seen, but no definite clubbed or branching processes were discovered. Similarly, scrapings from the bases of small superficial ulcers of the cecum near the cecal valve, showed similar forms.

Liver: Enlarged. At the attachment of the falciform ligament some purulent lymph was noted over a thickened capsule.

Gall-bladder: Normal. Portal vein large. Walls smooth. No evidence of thrombosis. Along its course, however, the main lesion of the organ was noted. Along the right portal, shortly after its origin, a large yellow semisolid area occurred completely surrounding vessel and showing extensive necroses of liver cells for some distance.

CASE 11.—Superintendent of car works, male, aged forty-seven years, residing at Nova Scotia. Seat of disease, appendix. Duration of symptoms before admission, one year. Admitted, January, 1908.

Chief Features of Illness. At first complained of indefinite pain in lower half of abdomen, with loss of appetite. Slight diarrhea. Typhoid fever diagnosticated. Remained in bed two weeks. On getting up found thigh flexed; unable to straighten it. Mass discovered in right lower quadrant. One month ago had a severe attack of pain, accompanied by vomiting. Incision made in mass; small quantity of pus escaped. Wound would not heal. Abscess appeared in loin. Lost weight.

Treatment. Incision in abscess; gauze packing. Potassium iodide internally.

Result. Died one month after leaving the hospital.

Remarks. No evidence of liver or lung complications. No autopsy.

CASE 12.—Student, male, aged ten years, residing at Montreal. Seat of disease, abdominal wall. Duration of symptoms before admission, six weeks. Admitted, February, 1908.

Chief Features of Illness. Onset similar to acute attack of appendicitis with crampy pains particularly in lower right quadrant radiating into loin. Bowels constipated. No vomiting. Right lower quadrant more prominent than rest of abdomen; a tender firm mass, which apparently only involved abdominal wall.

Treatment. Incision into mass. Tissue hard, almost cartilaginous. Little bleeding or pus. Condition entirely extraperitoneal. Potassium iodide.

Result. Cured.

Remarks. The organism in this case was never isolated.

CASE 13.—Clerk, male, aged twenty-five years, residing at Montreal. Seat of disease, appendix and wall of thorax. Duration of symptoms before admission, five years. Admitted, September, 1907.

Chief Features of Illness. Appendix removed five years ago. Fecal fistula developed and did not close for about a year, during which time a small quantity of blood-stained serum exuded. One year later a mass on the right side of the thorax appeared, which broke through the skin, leaving a sinus which has discharged at intervals for the past four years. On entrance to the hospital the appendix scar was healthy and the abdomen quite free. A small sinus was found over the lower part of the thorax in the middle axillary line.

Treatment. Incision along the sinus, which did not go through the parietal wall. Curetted. Packed with gauze. Potassium iodide internally.

Result. Cured.

Remarks. Here is a definite case of the entrance of the organism *via* appendix, which later healed and infection was still active in the thorax.

LEFT LOIN AND THORAX.

CASE 1.—Farmer, male, aged thirty-one years, residing at Montreal. Seat of disease, thorax, lumbar region. Duration of symptoms before admission, six months. Admitted, March, 1906.

Chief Features of Illness. Six months previously had an injury to the left side. Shortly after a small, painful mass appeared over the tenth rib in the middle axillary line. Incision by local doctor.

Small amount of pus evacuated. No loss of weight, cough, or expectoration. Readmitted in June, 1906. Small abscess near old scar. By this time some cough and expectoration. Evidence of thickened pleura over left base. Readmitted in January, 1908. Sinus well opened up. Curetted down to region of 12 D. V. In February left leg became flexed; mass appeared in loin.

Treatment. Excision of ninth and tenth ribs, both of which were apparently normal. A small sinus tracked into the pleural cavity, running in toward the spine. Curetted, packed with gauze. On readmission in June, curetted; no evidence of dead bone; disease seemed situated only in soft tissues. Potassium iodide given; iodide gauze packing. On readmission in January, 1908, packed with gauze. Potassium iodide internally.

Result. Died January, 1907.

Remarks. Autopsy at home incomplete. Actinomycosis found in pus, but never in sputa. Great emaciation, with deep yellow color of fatty tissue. Pleura thickened at base and contained a small amount of blood-stained serum. The sinus in loin and chest wall did not go deep but seemed quite superficial, leading down in case of thorax to the excised ribs.

CERVICOFACIAL SERIES.

CASE 1.—Bricklayer, male, aged thirty-seven years, residing at Montreal. Seat of disease, jaw and cheek. Duration of symptoms before admission, one year. Admitted, October, 1908.

Chief Features of Illness. Small mass appeared in the cheek on the right side near angle of the jaw. Lanced. Healed. Shortly afterward another appeared. Treated similarly and healed. Again near angle of jaw another mass appeared, with characteristic purplish skin over it, discharging a small amount of blood-stained pus.

Treatment. Incision. Curetting. Packing with gauze. Potassium iodide internally.

Result. Cured.

Remarks. Not diagnosticated for some time, until finally the ray fungus was isolated.

CASE 2.—Steamfitter, male, aged twenty-nine years, residing at Montreal. Seat of disease, jaw. Duration of symptoms before admission, three months. Admitted, October, 1908.

Chief Features of Illness. Small firm nodules near decayed molar of lower jaw. Swelling involved cheek; softened, with characteristic color of skin over it.

Treatment. Excision. Tooth extracted. Potassium iodide.

Result. Cured.

Remarks. Patient never had any further trouble six months after operation.

CASE 3.—Farmer, male, aged forty-four years, residing at Ontario. Seat of disease, submaxillary region. Duration of symptoms before admission, two months. Admitted, November, 1908.

Chief Features of Illness. Small tumor in submaxillary region just in front of angle of jaw. Gradually increased in size. Skin over it became purplish. Mass seemed to have no connection with mucous membrane of mouth. Lower teeth decayed.

Treatment. Teeth extracted. Mass excised.

Result. Cured.

Remarks. No further trouble.

CASE 4.—Farmer, male, aged thirty-one years, residing at Ontario. Seat of disease, cheek. Duration of symptoms before admission, two years. Admitted, December, 1908.

Chief Features of Illness. Neuralgic pains of upper jaw. Four months later abscess appeared. Incision; portion of dead bone removed. Attacks recurred. Several operations, curetting, etc. Small sequestrum removed.

Treatment. Incision. Drainage. Packing with gauze.

Result. Cured.

Remarks. Organism never found. This case looks more like active osteomyelitis than actinomycosis.

CASE 5.—Electrician, male, aged twenty-two years, residing at Saranac Lake. Seat of disease, cheek. Duration of symptoms before admission, three years. Admitted, May, 1909.

Chief Features of Illness. Small mass appeared near left molar from which a little pus oozed out. Tooth extracted and abscess healed. In region of old abscess the cheek became involved. Tooth in neighborhood, which was in bad condition, removed. Mass softened. Sinus formed. Skin was the characteristic color.

Treatment. Mass excised. Potassium iodide internally.

Result. Cured.

Remarks. Unable to trace patient.

CASE 6.—Merchant, male, aged twenty-nine years, residing at Ontario. Seat of disease, cheek. Duration of symptoms before admission, one month. Admitted, November, 1909.

Chief Features of Illness. Pain in right lower jaw. Small hard mass appeared in front of angle. Two weeks later face swollen. Mass firm. No evidence of fluctuation. Skin over it reddish purple color.

Treatment. Incision. Packed with gauze. Potassium iodide internally.

Result. Cured.

Remarks. Small quantity of blood-stained pus showed granules.

CASE 7.—Farmer, male, aged thirty-one years, residing at Ontario. Seat of disease, cheek. Duration of symptoms before admission, one year. Admitted, August, 1905.

Chief Features of Illness. Swelling of the cheek over the malar bone. A small sinus formed discharging pus into the mouth. Involved the cheek. Opened on the inner side, but still would not heal.

Treatment. Roots of teeth extracted. Free incision and curetting from outside. Packed with gauze. Potassium iodide internally.

Result. Cured.

Remarks. Two years after was well.

CASE 8.—Male. Seat of disease, cheek. Duration of symptoms before admission, six months. Admitted, April, 1905.

Chief Features of Illness. Wore plate which did not fit well. Near root of old wisdom tooth, small abscess formed. Tooth extracted. Condition improved. Finally cheek became very much swollen again with purplish discoloration of skin.

Treatment. Excision of mass. Potassium iodide internally.

Result. Cured.

Remarks. No further trouble.

CASE 9.—Lawyer, male, aged twenty-four years, residing at New Brunswick. Seat of disease, jaw. Duration of symptoms before admission, three months. Admitted, April, 1904.

Chief Features of Illness. A small abscess appeared opposite the molar teeth (lower). Incised. A small quantity of pus evacuated. Cavity closed. Two weeks later another similar one appeared. This time it quickly involved the cheek. Central portion soft, dark, reddish-purple in color. The surrounding parts firm, infiltrating. Incision made through cheek down to jaw. A small sequestrum removed. In June reëntered the hospital, with large fluctuating area in front of old scar. Skin over it a dark purplish color. Tender. No glandular involvement. Abscess appeared in right side of neck, also another on left cheek.

Treatment. Incision. Sequestrum removed. Wound healed. On readmission incision along inferior border of jaw; drained. Incision, packed with gauze. Potassium iodide internally. *X*-rays had a decidedly bad effect; small abscess seemed to form more quickly. Protonuclein, t. i. d.

Remarks. Early diagnosis of acute osteomyelitis. Later actinomyces found. This patient was operated on in all about one hundred times in various parts of the country. The disease extended down both sides of neck. The last operation occurred on October 11, and from that time on he was entirely free from the disease up to the time of his death, which occurred in June, 1911. Death from nephritis, due perhaps to ether-chloroform, or possibly excessive potassium iodide treatment, 60 gr., t. i. d.

CASE 10.—Nurse, female, aged twenty-five years, residing at Montreal. Seat of disease, jaw and cheek. Duration of symptoms before admission, one year. Admitted, October, 1904.

Chief Features of Illness. Small abscess appeared opposite the second molar at the junction of the cheek and the jaw. Discharged small amount of pus at intervals. Cheek finally involved. Characteristic discoloration of skin.

Treatment. Tooth extracted. Mass excised. Potassium iodide internally.

Result. Cured.

Remarks. This nurse attended patient No. 9.

CASE 11.—Wife of a farmer, aged twenty-two years, residing at Ontario. Seat of disease, jaw and cheek. Duration of symptoms before admission, one month. Admitted, October, 1904.

Chief Features of Illness. Began as firm nodule near lower right wisdom tooth. Incised; a small quantity of pus evacuated. Abscess reformed and opened again. Finally involved the cheek, with characteristic reddish-purple color.

Treatment. Infected area curetted. Teeth extracted. Potassium iodide internally.

Result. Cured.

Remarks. No recurrence.

CASE 12.—Wife of farmer, aged thirty years, residing at Ontario. Seat of disease, jaw and cheek. Duration of symptoms before admission, three months. Admitted, November, 1904.

Chief Features of Illness. Small swelling opposite left lower wisdom tooth. Varied in size. Tooth extracted. Disappeared but reappeared shortly afterward. Cheek became involved. Skin over central part had the characteristic color.

Treatment. Teeth extracted. Mass excised.

Result. Cured.

Remarks. No recurrence.

CASE 13.—Plumber, male, aged fifty-four years, residing at Montreal. Seat of disease, jaw and cheek. Duration of symptoms before admission, three months. Admitted, January, 1912.

Chief Features of Illness. Last left lower molar extracted. Face became very much swollen just below angle of jaw. Incision into mass; found very firm with cartilaginous appearance. Little bleeding and small amount of serosanguinous pus and granules. Over one softened area there was the characteristic purplish color of skin.

Treatment. Incision. Packed with iodoform gauze. Potassium iodide.

Result. No improvement.

Remarks. This is a recent case, and has not had time for any definite development.

CASE 14.—Thresher, male, aged twenty-four years, residing at Montreal. Seat of disease, cervical glands. Duration of symptoms before admission, two months. Admitted, December, 1911.

Chief Features of Illness. Small, hard lump appeared on right side of neck in front of the sternomastoid below angle of the jaw. Firm, not painful. Increased gradually in size. Gives history of chewing straws. Teeth in lower jaw all decayed.

Treatment. Several operations. Incisions. Gauze packing. Washing with weak solution of iodine. Potassium iodide internally.

Result. No improvement.

Remarks. A recent case; not long enough time to give result. Was not diagnosticated for some time. Small amount of sero-sanguinous pus.

CASE 15.—Clerk, male, aged twenty years, residing at Montreal. Seat of disease, cheek. Duration of symptoms before admission, two months. Admitted, April, 1908.

Chief Features of Illness. Small abscess appeared near lower right molar teeth, which were not in good condition. Mass lanced by dentist; small amount of pus escaped. Condition did not improve. Finally cheek involved. Central part softened and skin over it had a peculiar dusky red color.

Treatment. Opened. Curetted. Packed with gauze. Teeth extracted. Potassium iodide internally.

Result. Cured.

Remarks. After-history not obtainable.

CASE 16.—Female, aged nineteen years, residing at Ontario. Seat of disease, cheek. Duration of symptoms before admission, one month. Admitted, December, 1905.

Chief Features of Illness. Toothache in upper left molars. Teeth had been treated previously. Gum-boil appeared. Lanced by dentist; disappeared, leaving an indurated mass. Injured cheek in this area and became immediately swollen. On entrance to the hospital central part of swelling was soft, with characteristic color. Evidence of fluctuation.

Treatment. Teeth extracted. On roots of molars small abscess sacs were noted. Excision of cheek tissue. Packed with gauze. Potassium iodide internally.

Result. Cured.

Remarks. Injury here seemed to light up the process.

CASE 17.—Grain merchant, male, residing at Ontario. Seat of disease, cheek. Duration of symptoms before admission, two months. Admitted, December, 1905.

Chief Features of Illness. Mass appeared in gum near bad teeth which were removed. Incision by dentist. Small amount of blood-stained pus escaped. On entrance to the hospital skin of the cheek was slightly involved.

Treatment. Curetted. Packed with gauze on two occasions. Potassium iodide internally.

Result. Cured.

Remarks. No recurrence.

CASE 18.—Male, aged forty-two years. Seat of disease, cheek. Duration of symptoms before admission, two months. Admitted, December, 1905.

Chief Features of Illness. A small mass appeared in left cheek, the size of a bean, gradually increasing in size, and becoming soft, dark purplish-red in color. On incision a small quantity of blood-stained purulent material escaped, leaving a discharging sinus.

Treatment. Excision. Potassium iodide internally.

Result. Cured.

Remarks. Sent to the hospital as tuberculosis. (Usually no diagnosis sent with these cases.)

CASE 19.—One case in O. D. department. Incised, packed with gauze, but patient never returned for further treatment.

GROIN CASES.

CASE 1.—Wife of farmer, aged twenty-nine years, residing at Ontario. Seat of disease, left groin. Duration of symptoms before admission, two months. Admitted, March, 1903.

Chief Features of Illness. Pain in lower left quadrant, with frequency of micturition. Two weeks ago mass appeared in groin above Poupart's ligament. History of diarrhea for some time past. Urine normal.

Treatment. Incision; packed with iodoform gauze. Potassium iodide internally. Discharged.

Result. Cured.

Remarks. Never established any relationship with bladder. Two years later a small abscess developed near scar, which was opened by her doctor, curetted, and potassium iodide given internally. Since then she has been perfectly well.

CASE 2.—Housework, female, aged forty-eight years, residing at Montreal. Seat of disease, left groin. Duration of symptoms before admission, two months. Admitted, January, 1908.

Chief Features of Illness. Complained of weakness and loss of weight. Five weeks ago noticed pain in left lower quadrant which lately had been very severe. Twelve days ago a small mass appeared in left groin, the centre of which is soft while the periphery is firm and hard and infiltrates the abdominal wall. Bowels constipated.

Treatment. Incision. Small quantity of foul-smelling pus escaped. Packed with gauze. Drainage. Potassium iodide internally. Discharged.

Result. Cured.

Remarks. Apparently entirely in abdominal wall. Foul odor due to colon infection. (No mention of hemorrhoids or other lesions about the rectum or the anus in this case.)

CASE 3.—Cheesemaker, male, aged twenty years, residing at Province of Quebec. Seat of disease, left groin. Duration of symptoms before admission, six months. Admitted, August.

Chief Features of Illness. Began with pain of dull aching character in epigastrium, which later localized to left lower quadrant. Pain became very severe, and mass appeared just above Poupart's ligament. Patient walked with limp.

Treatment. Incision. Evacuated blood-stained seropus containing numerous granules. Packed with iodoform gauze. Potassium iodide internally.

Result. Improved.

Remarks. Left the hospital with sinus. Later information could not be obtained. (No mention of hemorrhoids or lesions about the rectum or the anus in this case.)

SKIN CASE.

CASE 1.—Laborer, male, aged thirty-six years. Seat of disease, skin. Duration of symptoms before admission, one year. Admitted, September, 1905.

Chief Features of Illness. Began as small callous spot at inner part of thenar eminence of right hand; about the size of a split pea when first noticed. Cracked and exuded a small quantity of blood-stained serum. Finally a definite ulcer formed which was cauterized and excised. Small ulcer returned in scar, beginning as small vesicle outside of which more vesicles occurred; gradually coalesced, forming large ulcer; base, dark red covered with sloughy material. Skin in neighborhood dark blue color.

Treatment. Excised. Potassium iodide internally.

Result. Cured.

Remarks. Organism never isolated.

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HEMA-URO-CHROME:

A NEW LABORATORY TEST FOR CANCER AND SARCOMA, ALSO A METHOD OF SEPARATING BILE ACIDS AND PIGMENT WITH THE APPLICATION OF TORQUAY'S TEST, INDICAN BEING OBTAINED IF PRESENT. A PRELIMINARY REPORT.

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Urine, being a secretory excretion, has from time immemorial been subjected to more or less inspection and examination, as affording clues to pathologic conditions in various tissues and organs of the body. As is usual in all progressive studies, while the substances found have remained the same, the interpretation has changed with increased knowledge. Albumin in the urine does not signify Bright's disease; indeed, I doubt if many physicians of today have read Bright's classic. It is not a common disease of the kidney, and in many text-books the description is greatly confused. Neither do the albumoses, or Bence-Jones body, signify chronic suppuration or disease of the bone-marrow, for they are found in many diseased conditions, especially in those of malignant or "near malignant" character. Many tests for bile in the urine have been proposed, and during years of experience in the examination of urine I have had opportunity to try them all. Most have been unsatisfactory and uncertain, even when the bile acids and coloring has been obtained in a concentrated form by the following method (which is, so far as I am aware, original).

To 100 c.c. urine in a flask of about 150 c.c. capacity add 10 c.c. hydrochloric acid; heat over a slow fire until ebullition begins. Remove from the fire and when cool add 30 c.c. ether. Agitate occasionally by turning the flask, avoiding hard shaking, which interferes with removal of the ether. After about twelve hours remove the ether into a clean white dish; allow it to evaporate spontaneously, when the bile acids and coloring matter will be left upon the bottom of the dish. The bile acids may be converted into salts by the addition of a small amount of a 1 per cent. solution

of sodium acid-carbonate (bicarbonate) in water and the several tests applied.

Some four years ago my attention was attracted to Torquay's test, which is a recently prepared solution of methyl violet, 1 to 2000 of water. (Practically one drop of the saturated alcoholic solution in an ounce of water.) Two tubes of equal size are partly filled with this solution; to one is added a small amount of the above solution of bile, which discharges the blue tint leaving the red. Comparison of the tubes renders the color change very distinct. Indeed, it is the most distinctive test for bile I have used. Having verified its reliability, which has also been done by a German observer, using the several substances obtained from urine, I can commend it.

Indican if present will be seen on the white dish as a ring above the bile acids and coloring. After chloroform or ether anesthesia, acicular crystals of ammonium chloride will be deposited and in some pathologic conditions cystin and fatty substances found. During the use of this method I would occasionally find the ether pink, even red in color and upon evaporation a more or less heavy deposit of hematin would be seen above the indican and constituents of bile.

Observations extending over more than four years lead me to state that this pink coloration may occur to a slight degree in diseased conditions of the liver when the hepatic cells are unable to convert the product of the lysis of erythrocytes into bile acids and coloring substances; therefore it occurs in cholemia from any cause and in jaundice, especially the hematogenous form. It will be found when the urine contains red blood cells from any cause, whether acute nephritis or hemorrhage, from some portion of the urinary tract. These may be differentiated by the microscope and removed before further testing. The pink tint appears due to a cleavage product of hemoglobin, probably hematin, and is present in larger amounts in the several infectious fevers, malaria in all its forms, greater in the severe types, as in the "tick-fevers" of Central America and Mexico, in babesia, piroplasmosis, etc. In the urine of a woman from Yuma, Arizona, with anemia, the hemoglobin content being only 35 per cent., in whose blood a spirillum staining blue with Giemsa was found, the hematin was strongly positive.

Hematin will be present in the urine of the anemias associated with tapeworm, uncinariasis or hook-worm, and other intestinal parasites. It will be present in greater amount in the anemias due to disease of the blood-making organs, and in the essential anemias due to near malignant disease of the lymph and ductless glands, especially in hyperthyroidism and in splenic, myelogenous, and pernicious anemia, the hematin being in proportion to the destruction of erythrocytes. While the tint and depth of color

will vary with the proportions of bile, indican, hematin, and urochrome present, by far the greatest amount and intensity of color obtained by the process described was found in the urine of patients suffering from malignant disease, cancer and sarcoma. *I have never found it absent in cases of cancer or sarcoma* even when of small size or unsuspected.

So far as possible all the cases hereafter mentioned have been subjected to the pathologic test, after clinical, surgical, and laboratory examinations, that the statements made might be verified.

The urine of these patients does not differ macroscopically from normal urine; it is not smoky as is urine containing blood, nor reddened, as in hemoglobinuria.

By the process described, a deep red urochrome is liberated by the action of hydrochloric acid and heat and taken up by the ether.

Chemical and spectroscopic examinations indicate that it is derived at least in part from the red-blood cell, but there is in the urine of patients suffering from cancer and sarcoma a substance other than hematin; but as the chemistry of the urochromes is so involved and contradictory, I hesitate to affirm its composition.

It appears from the evidence obtained to belong to the tryptophan, pyrrol or indol group, possibly indoxyl red, hence we may regard this red urochrome as a mixture or combination of hematin and an indoxyl base, produced by the lysis of erythrocytes and the destruction of proteid by the cancer cell. That we might have a convenient term by which to express this substance and indicate its source, I have chosen tentatively the compound word, "hema-uro-chrome."

I have examined the urine from a number of cases of malignant growth not enumerated and have made control examinations of blood and urine almost innumerable during the past four and a half years. To indicate the variety of cases examined and the assistance rendered by friends I will cite the following: More than four years ago, being convinced of the presence of this hema-uro-chrome in the urine of cancer cases, I asked Dr. W. H. Dukeman, for a specimen of urine from a patient with cancer of the rectum, and found it strongly positive. Portions of the growth were examined by me and by Dr. C. C. Warden, pathologist, who confirmed the diagnosis of rectal cancer. Dr. Dukeman later brought a catheterized specimen of the urine from a case of continuous uterine hemorrhage, due to a suspected cancer of the uterine body. The hema-uro-chrome test being strongly positive, I concurred that a hysterectomy was indicated, the diagnosis being confirmed by the same pathologist. About three years ago Dr. Dukeman brought the urine from a patient suffering with sarcoma of the neck, which after examination, he pronounced inoperable. The patient went to Dr. W. A. Mayo, of Rochester, Minnesota, who after a surgical and pathologic examination declined to operate; in this case the

hema-uro-chrome test was markedly positive. It was strongly positive in sarcoma of the eyeball under the care of Dr. F. E. Detling. In a small epithelioma of the eyelid and in two cancers of the pharynx under the care of Dr. H. A. Kiefer, the relative quantity was surprisingly great. In cancer of the tongue the tumor being removed by Dr. Granville MacGowan, the test was positive and traces remained in the urine for more than three months, gradually disappearing. This growth was *very small* and Dr. Stanley P. Black, who made the pathological examination, stated, "It was in the very beginning difficult to find and determine the true nature." Dr. Black had opportunity to apply the test where, after removal of a breast for cancer, recurrence with metastasis to bone and omentum occurred; confirmed by autopsy. Here the hema-uro-chrome was present in large amount. I have advised operation for mammary cancer when the growth was so small the surgeon hesitated to operate, upon a positive finding of the hema-uro-chrome, being justified later by the pathologist. I have had urine from many cases of cancer of the face, lip, and jaw of small and large size through Drs. Edwards, MacGowan, Crum, Stoner and others, all of which were positive. Through the kindness of Dr. Shippey, of the Soldiers' Home, and Dr. M. G. Gates, from the County Hospital, I have had many specimens with extensive involvement, metastasis, or general carcinomatosis; the amount of the hema-uro-chrome bore a distinct relation to the extent of the cancer process. I had opportunity to apply the test with positive results in cancer of the thyroid, causing necrosis of the tracheal cartilages and death, through the courtesy of Dr. Sutton, of Zanesville, Ohio. Through the courtesy of Drs. MacGowan, Dillingham, Hart, and others several specimens of urine, where cancer of the bladder was under consideration, gave negative results, confirmed by cystoscopy or operation. Also, two cases of cancer of the sigmoid were strongly positive, as was an unsuspected cancer of the transverse colon.

Two cases difficult of diagnosis, cancer being under consideration, in the practice of Dr. William A. Edwards, one being a pathological condition affecting the transverse colon, the other the stomach, gave negative results as to the hema-uro-chrome, but strongly positive reactions for bile by Torquay's test; which suggested the possible elimination of cancer by the test, thereby extending its application. Dr. A. F. Zimmerman had under his care a man presenting the symptoms of pyloro-duodenal cancer, the urine being negative as to hema-uro-chrome, but strongly positive to Torquay's test, with a large yield of bile-acids and pigment. I suggested a differential diagnosis of duodenal ulcer near the papilla, causing obstruction with resorption of bile. These cases indicate that the test may be used as a means of differential diagnosis. It presents to us three substances of pathological importance: bile, indican, and the hema-uro-chrome, each having a distinct significance.

I am not aware of the previous application of the uro-chromes in the diagnosis of disease. That the greater number of them represent pathologic metabolism, especially when in excess, there can be little doubt.

It has long been known that cancer cells produce ferments or enzymes which cause hemolysis, cytolysis, and proteolysis. It is upon this fact that all serodiagnostic methods are based; hence the method I propose has a foundation similar to the methods of Salomon-Saxl and Salkowski, as well as the meiostagmin reaction. None are absolutely specific for cancer, but are suggestive, and will sustain a wavering diagnosis, being positive in at least 85 per cent. of cancer cases and present in only 15 per cent. of other diseases.

The method proposed by me is more simple, easy of execution, and less liable to error than any of the others, and other diseased conditions yielding hematin can be eliminated by methods known to all. That they may be compared, I have epitomized the best of these methods recently proposed.

Salkowski put forward colloidal nitrogen when found in the urine in excess of normal (3.42 per cent.) as diagnostic of cancer, and many careful observers since have agreed that colloidal nitrogen of 6 to 7 per cent. is positively diagnostic of cancer.

Mancini, however, calls attention to the fact that colloidal nitrogen passes into the circulation and is eliminated by the kidneys in larger proportion than normal in many morbid conditions. He found this to occur in pulmonary tuberculosis, in many suppurative processes, in pleurisy, and in cirrhosis of the liver when the exudate is being absorbed, but not in so large a proportion as in cancer.

Caforio corroborates this statement, and states that the excess of colloidal nitrogen gradually disappears after excision of the cancer. The method of estimating colloidal nitrogen is as follows: If the urine is alkaline it is rendered slightly acid with acetic acid. If it contains albumin this is removed by boiling. After filtration the total nitrogen in 5 c.c. of the twenty-four hour urine is determined by Kjeldahl's method. One hundred c.c. of the same specimen is evaporated upon a water-bath to 10 c.c. cooled, and 100 c.c. of absolute alcohol added to precipitate the colloidal nitrogen. After standing several hours it is thrown upon a filter and the precipitate washed with alcohol until all traces of urea are removed. The precipitate is then dissolved in hot water and the nitrogen determined by Kjeldahl's method, from which the colloidal nitrogen can be determined.

Salomon and Saxl found increase of the sulphur-containing oxyproteids in the urine of more than 70 per cent. of cancer cases, even in those well nourished; while in 150 control cases they found only one which showed such increase, and that in a moribund case

of cirrhosis of the liver. After removal of the sulphates by barium chloride they propose to oxidize the neutral sulphur-containing oxyproteids by hydrogen peroxide then to estimate the sulphates, in this manner determining the sulphur oxyproteids.

Breiger's antitrypsin test is not specific, but negative findings appear to exclude cancer.

Among recent reactions of the stomach contents, Salomon's test has proved valuable, frequently disclosing an unsuspected ulcerating gastric cancer, although a benign ulcer may occasionally give the reaction. The technique is as follows: For a day before the test is to be made the patient does not eat anything containing albumin and restricts himself to fluids. In the evening the stomach is washed out with 400 c.c. of decinormal salt solution, and again in the morning with the same amount. The latter is tested for albumin by Esbach's method and for nitrogen by Kjeldahl's method. If positive to Esbach's and 20 mg. of nitrogen are found by Kjeldahl's it is evident an ulcerating cancer is present, although a benign ulcer has given the reaction.

Salomon and Falk's salicylate test is one of the latest contributions to the diagnosis of gastric cancer. The stomach of the fasting patient is washed out, after which a rectal enema containing 3 gm. sodium salicylate is given. As soon as salicylic acid can be detected in the urine the stomach is washed out and the rinsings tested for salicylic acid. While salicylic acid cannot be detected in the rinsings from a healthy stomach, and rarely in those from one with benign ulceration, it is found in the rinsings from an ulcerating cancer.

The glycyltryptophan test is liable to error, because of regurgitation of the duodenal contents as well as the presence in the saliva of a peptidolitic enzyme.

According to Freund and others the meiostagmin reaction is simple and reliable. In this, advantage is taken of the cancer cells' destroying power of normal blood serum; but difficulty is often experienced in obtaining suitable cancer-cell material, for in many cases cancer cells are not destroyed by serum. The basis of the reaction is the fact that when the antibodies of a disease and the corresponding antigens are brought together there is a lowering of surface tension in the mixture, with a change in the rate of dropping of the fluid from the stalagmomometer, as the special pipet is called.

Izar has lately reported upon a meiostagmin inoculation reaction, the findings of which were positive when the original meiostagmin reaction failed. He found that an aqueous emulsion of an ether or methyl-alcohol extract of malignant tumors heated to 50° C. (122° F.) acquired extremely toxic properties. When a mixture of such an extract and blood serum is centrifuged the toxic properties are concentrated in the supernatant fluid in the non-

malignant cases, while in sarcoma or cancer it remains in the sediment. Furthermore, this sediment suspended in salt solution and injected into rabbits caused their death in twenty-four hours. This he calls the "meiostagmin reaction *in vivo*."

This brief review of recent work in the diagnosis of cancer will emphasize the simplicity of the test I propose.

It has long been recognized that any treatment of cancer, to be successful, must be instituted early in its existence, the earlier the better. It is for this reason that many have endeavored to find a laboratory test which would give assurance that a suspicious tumor growth was malignant, and its removal justifiable without cutting into it, that a portion might be obtained for microscopic examination.

Bergel calls our attention to the fact that early in the existence of a sarcoma or cancer tumor it is surrounded by a zone of inflammation, as is any foreign body, this being the natural attempt of the organism to protect itself. So long as this barrier is unbroken the cancer cells are not disseminated; but when this protecting wall is broken by feebleness of cell resistance or by traumatism, extension by contiguity or by metastasis will occur. He calls attention to the fact that horse serum has a tendency to deter the growth of cancer cells.

Investigating the use of serum, he found that fibrin was the only constituent which gave rise to a typical aseptic inflammation, with great leukocytosis, serous or fibrinous exudation, with fibroblasts and the formation of new connective tissue without producing anaphylaxis or other ill effects. He found that injections of pure fibrin (in the form of Merck's substitol, 5 grains of which are equal to two and a half fluidounces of serum) not only inhibited the growth of the cancer but caused a definite shrinkage of the tumor. The substitol was suspended in salt solution.

More recently Wassermann, working with Keyser and M. Wassermann upon "mouse cancer," found an eosin-selenium compound, which has the power of causing softening, distintegration, and absorption of such malignant tumor. Wassermann found that eleven daily injections of this eosin-sodium-selenium compound into the caudal vein of white mice caused the disappearance of the tumor without recurrence, but earlier interruption of the treatment was followed by recurrence of growth. If the tumor was not larger than a hazelnut no untoward effects occurred, but the softening and absorption of a large growth could but of necessity produce untoward effects not only from the selenium or tellurium, but from the hemolyzed tumor products. Wassermann cautions us that "this product has not as yet been applied to man," neither has the mode of preparation or its composition been made public. However, its successful use in "mouse cancer and sarcoma" without recurrence justifies the hope that some

similar substance may be found and applied to the treatment of malignant disease in human beings. Such treatment must of necessity be instituted early in its existence. This depends upon an early diagnosis.

No certainty exists as to the origin of these neoplasms, the ignorance upon the question being almost appalling. The fact that I have never failed to find this hema-uro-chrome present in cancer furnishes my excuse for presenting this prelimenary report.

Wassermann's treatment is based upon the following facts: Heliotropism of cells and collections of cells constituting vegetable and animal life has long been recognized and the chemical activity of the more refrangible rays from blue to the ultra-violet is well-known to be greater than the yellow and red rays, a fact utilized in the various "light treatments." It is but reasonable to suppose that the red rays lessen the activity of nuclear division or mitosis and have a tendency to produce a more resistant cell, a condition observed after the use of Ponceau, also known as Schaarlach and Beibrich's red. It was observed by Wassermann, working with Ehrlich, several years ago, upon "dye stuffs," that cells derived from the epiblast had a strong chromo-chemo-taxis for dyes of the fluorescin group, especially for eosin, which led him to employ eosin as a carrier for the cell-destroying selenium and tellurium. He bases his use of selenium and tellurium upon the findings of Gosio, who about four years ago found selenium and tellurium, or their salts, a reliable method of differentiating degenerating and dead cancer cells from living cells, an almost black precipitate being deposited about the nucleus of degenerating or dead cells. Both Gosio and Wassermann are apparently ignorant of the fact that homeopathic experimenters or observers called "provers," more than thirty years ago, found that selenium and tellurium as well as their salts have selective affinity for cells derived from the epiblast. Selenium affects them less than the more powerful tellurium, which causes degeneration and death of epidermal cells as well as of nerve endings in the deeper layers of the skin, affecting even the spinal nerves, extending from the seventh cervical to the fifth dorsal. It may be recalled that these supply practically all the muscles of respiration, including accessory muscles. Large doses cause death by asphyxia; for the authenticity of which I refer to Richard Hughes.[1]

Selenium and tellurium are non-metallic elements of the sulphur group. They form oxides, acids, and salts similar to sulphur, but appear to have a more destructive effect upon cells derived from the epiblast, especially if irregular or atypical. The success of Wassermann's work upon mouse cancer gives hope that a similar substance may be found of service to man, but to be of service it

[1] Manual of Pharmacodynamics, 1886, 5th ed., p. 803.

must of necessity be used early in the development of the tumor or malignant growth. Hence an early diagnosis is imperative. For that reason I present this test, with some of the evidence, trusting it may be of service. It is easily applied and based upon a sound foundation, viz., the passing into the circulation and elimination with the urine (a natural excretion) of the products of hemolysis, cytolysis, and proteolysis by the cancer cell during its growth and extension.

In cancer the amount of the hema-uro-chrome must of necessity vary with the activity and extent of the cancer process, and I do not believe a percentage proportion would be of value if determined. I have therefore depended upon the relative amount of the hema-uro-chrome obtained from a definite quantity of urine by a certain amount of hydrochloric acid and ether.

I hope that which I have presented will aid in the diagnosis of cancer at a period when removal by operation or some form of medication may rid the individual of a terrible menace.

Beside, a negative finding will enable us to relieve that mental distress associated with a suspicion of cancer or of its recurrence.

A PSYCHOSIS FOLLOWING CARBON-MONOXIDE POISONING, WITH COMPLETE RECOVERY.[1]

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Among the various toxic psychoses which have come under my observation in the Government Hospital for the Insane, one which was produced by carbon-monoxide poisoning is of special interest, in view of the fact that the patient suffered from a severe intoxication which resulted in the development of mental symptoms one month following the accident, and terminated in a complete recovery. That psychic disorder is one of the sequels of this form of poisoning has long been recognized, yet few cases have been recorded in this country. A careful review of the literature yields scanty information as to the clinical and pathological course of this toxemia, notwithstanding many accidents occur in our large cities and collieries. However, some valuable observations on this subject can be obtained from foreign publications.

Cases of carbon-monoxide poisoning may be accidental, suicidal, or homicidal, or the latter two may be combined. In France four-fifths of the suicides are caused by poisoning with carbon-

[1] Read at the International Congress on Hygiene and Demography, 1912.

monoxide gas. In the large cities of this country scarcely a day passes without a number of cases are recorded of accidental or suicidal intoxication from this gas. According to the daily papers in New York City alone there were reported to the coroner in the first six weeks of the present year seventy-five fatalities. Deaths by gas poisoning have been steadily increasing for the past twenty-five years, and this increase has been due to the manufacture of illuminating gas by a method known as "water gas." This gas has come to be such a serious cause of death, that a point has been reached where it behooves the health authorities and others interested in the subject to consider what steps can be taken to curtail this mortality. However, at present there are no available statistics of these accidents or fatalities. The last "Bulletin of the United States Census Bureau on Mortality Statistics" does not group these deaths independently, but includes them under the general head of Mortality from Intoxication. In 1910 the Bureau of Commerce and Labor issued a Bulletin on "Fatal Accidents in Coal Mines." This report furnishes no information concerning the effects of such intoxication upon those who escaped death.

In recent years many of the States have appointed commissions to investigate occupational diseases, and in 1909 these commissions united as a permanent organization known as the National Conference upon Compensation for Industrial Accidents, with the object in view to obtain uniform legislation for men engaged in dangerous occupations. In connection with this the International Association for Labor Legislation has prepared a plan for the protection of workmen exposed to the dangers of industrial poisons in order that they may be able to get adequate legislation regulating the same. A committee of this society has compiled a list of these industrial poisons, and recently the United States Department of Commerce and Labor has published the following tabulated list, which deals with the source, chemical and physical properties, and the industries in which the poisoning occurs, together with the toxic symptoms following exposure:

"Carbon monoxide is described as a colorless, tasteless gas, and when in a state of diffusion is odorless, burning with a blue flame in the air. Coal vapor has about 0.5 per cent. of carbon monoxide. Illuminating gas, 6 to 10 per cent. carbon monoxide and 33 to 40 per cent. of mine gas. Water gas, a mixture of 41 per cent. carbon monoxide, 50 per cent. hydrogen, 4 per cent. carbon monoxide, 2 and 5 per cent. nitrogen. Producer gas contains 34 per cent. carbon monoxide and 60 per cent. hydrogen gas.

"Branches of industry in which poisoning occurs: In industrial plants with defectively planned or ill-tended firing and heating arrangements; plants for the production of industrial gas; mining (mine gases); coal mines; blast furnaces (furnace gas); Cowper apparatus; gas purification; coke ovens; smelting furnaces; gas

machines; lime and brick kilns; dolomite calcining kilns; iron and metal foundries (drying of the molds); soldering in tin shops; charcoal burning; resin distillation; ironing; heating with open coal brasiers or coke stoves (drying the plaster and walls of new buildings); drying chambers."

Another source of danger from this gas has arisen in recent years from the extensive use of benzine and gasoline explosive engines, which are installed in the motor car, motor boat, and aeroplane. Investigations following accidental death from the gas escaping from such engines revealed the fact that the men attending the engines in the cabins of launches often have toxic symptoms—headache, dizziness, etc. In this connection it is the opinion of Surgeon-General Stokes, of the United States Navy, that noxious gases generated by exploded powder in the turrets, from burning coal in the fire rooms, and other gases similar to carbon monoxide in illuminating gas, are responsible for the collapse and sometimes death of men working in the above spaces.

To quote further from the Bulletin, the symptoms of acute poisoning are: "Increased blood pressure at first, with slowing of the pulse and pounding heart beat; later, lowering of the pressure, with rapid but small pulse, and, not infrequently, with discrete spots of dilatation in the superficial bloodvessels. Remarkably pale red discoloration of the blood and of the dilated spots; formation of carbon-monoxide hemoglobin is demonstrable by the spectrum. (*a*) Disturbances of the general health. In mild cases, dull headache; flashes before the eyes; giddiness; ringing in the ears; nausea and fulness in the gastric region. (*b*) In severe cases: Bluish discolortation of the skin; spasmodic, wheezing respiration; sometimes tonic and clonic convulsions; more often paralytic symptoms, either with weakness of all the extremities, or the lower only, or indeed of only single groups of muscles, including also the facial muscles. The convulsive stage, which may be altogether absent, is succeeded by the stage of asphyxia, with sensory and motor disturbances, involuntary voiding of urine, semen, and feces; subnormal temperature; weak, slow, and intermittent pulse; loss of consciousness. As sequels there have been observed pneumonias, inflammations of the skin, paralyses and psychoses, the last two often pursuing an unfavorable course. Chronic poisoning (among ironers, firemen, cooks, etc.): Frequent headaches; dizziness; nausea; vomiting; coated tongue; weakness of memory; anemia without chlorosis; "hot flushes;" formication; palpitation of the heart; insomnia; general debility and feebleness of the psychic functions."

Ziehen describes the chronic monoxide poisoning which affects those employed in laundries as ironers, firemen, and others who work in crowded, overheated places in which there are bad heating arrangements, and in which these people are obliged to remain

for some considerable time. It manifests itself in general nutritional disturbances, and presents a picture of mental and bodily fatigue which is sometimes regarded as either neurasthenia or hysteria.

The following is the clinical record of the case:

CASE No. 18,888.—M. A. O., aged forty-five years; native of Ireland; single; indigent; admitted December 10, 1910.

The following history was supplied by an aunt of the patient, with whom she made her home. After the patient's return to her normal mental state she corroborated this information.

Family History: Negative so far as could be learned as to nervous or mental diseases, epilepsy, etc.; mother died of tuberculosis at the age of thirty years.

Personal History: Born in Ireland; was elder of two children; always healthy; common-school education. After her mother's death kept house for her father until she came to this country, at the age of twenty-eight years. Upon her arrival in this country she obtained employment as a domestic, and was evidently an efficient servant, as she was employed for a number of years by prominent families in this city, including those of a United States Senator and a German Ambassador. She was of a cheerful disposition, habits good, and always attended to her religious duties. Was fond of reading history, fiction, periodicals, etc. On November 2, 1909, she went to bed in her usual good health, and the following morning was found in a deep coma. Upon investigation it was found that illuminating gas was escaping from a defective fixture in the room which she now occupied for the first time upon her return from her vacation, not knowing that the stop-cock was broken, though this fact was known by the other servants in the house. Had it not been for an open window the accident would probably have been fatal. She was at once removed to the George Washington University Hospital, where she remained in an unconscious condition for four days. The informant called on her four days after the occurrence, but at this time was unable to arouse her. However, on the sixth day the patient recognized her, although she was dull of comprehension and appeared somewhat somnolent. From this time on the patient daily improved, and was discharged November 13, 1910, having recovered from the acute effects of the poisoning.

Abstract of record from the George Washington University Hospital, where she was first taken immediately after the accident: Admitted to the George Washington University Hospital, November 3, 1910. For the first twenty-four hours patient's temperature fluctuated between 101° and 100°; pulse between 120 and 82; respirations 40 and 22. Was given oxygen on admission and normal salt solutions frequently, at least every four hours; hot applications externally. Patient began to perspire about three hours after

admission. She was given oxygen every hour for a short time. Hypodermoclysis of 500 c.c. was given.

Summary: At the end of first day: Nurses' notes: Was catheterized. Patient perspired a great deal. Hot bottles; oxygen every hour, for fifteen minutes during the last eighteen hours. Patient turned on her side for a half hour during the night.

Summary: At end of second day: Maximum temperature 101°, minimum 98.6; pulse 100 to 80; respirations 30 to 24. Oxygen given every hour, for fifteen minutes. Hot applications; normal salt injections. Nurses' observations: Patient restless all night; seemed more rational.

Summary: At end of third day: Maximum temperature 100°, minimum 99°; pulse 100 to 70; respiration 30 to 24. Oxygen given. Saline solution discontinued. Patient conscious at intervals; slept very little; complained of pain in back; very restless all night; slept at intervals.

Summary: At end of fourth day: Temperature normal; pulse 78° to 70°; respiration 26 to 24. Patient restless all night, complaining of pain in back and neck; slept about one hour. Patient tossed about the bed; got out of bed.

Summary: At end of fifth day: Maximum temperature 98.6° to 97.8°; pulse 80 to 78; respiration 28 to 24. Patient very quiet during the day; restless all night; complained of pain in back; asked to get out of bed. Slept from one o'clock on at intervals.

Summary: At end of sixth day: Temperature normal; pulse 80 to 74; respiration 24. Patient very restless all night; complained of pain in the back; wanted to get out of bed. Slept about three hours.

Summary: At end of seventh day: Temperature normal; pulse 80 to 74; respiration 24 to 22. Patient very restless all night; slept about four hours during night. Very nervous. Given regular diet; eats well. Voided urine.

Summary: At end of eighth day: Temperature normal; pulse 78 to 76; respiration 24 to 22. Patient very restless; slept about four hours during the night. Very nervous; given regular diet; eats well. Voided urine. Patient sat up in chair during the day.

Summary: At end of ninth day: Temperature normal; pulse 80; respiration 24. Patient up during the day; walked about; slept well.

November 13, 1910. Tenth day: discharged.

Upon her return to her aunt's home she continued to improve, and after two weeks was allowed to go back to the place where she had been working, as relatives and friends at this time considered her well. Soon after she resumed her duties the servants with whom she was associated noticed that she was becoming dull and forgetful about her work. She gradually became worse, and on

this account at the end of a week she was taken back to the home of her aunt, where she remained until her admission to this hospital.

While at her home, one week later, her aunt observed that her actions were peculiar; her movements were very awkward and her memory seemed to be a complete blank. She had outbursts of laughter without provocation; did a great many irrational acts; for instance one day she was noticed trying to put the trousers of a little boy on for a waist. She put her hands through the legs and tried to pull the trousers over her head. She was unable to find her way about the house. One day she wandered from her aunt's house to the United States Treasury Building, where she accosted a policeman and told him that she was in search of the house on U Street where she was formerly employed. She was directed to the residence and found her way there safely. A few hours afterward she was again taken back to her aunt's home. At this time she was oriented to person and place, but could not tell the hour, day, month, or year. Was unable to attend to her personal wants, became very untidy; would not remain in bed; and finally passed into a state of confusion and was brought to this hospital December 10, 1910, thirty-eight days after trauma.

On admission to this hospital, December 10, 1910, the patient was in a semistuporous condition; would answer questions promptly; was able to give her name, but all other replies were incorrect and irrational. She extended her tongue when told to do so, but otherwise was unable to carry out the simplest orders given her; was spoon-fed, as she was unable to feed herself. Throughout examination patient showed causeless laughter.

Physical Examination: Patient was in bed; well-nourished white woman; height five feet two and a half inches; weight 120 pounds; mask-like facial expression; hair dark brown mixed with gray, fine in texture; slight lateral scoliosis; deformity of sternum at articulation of the gladiolus with the manubrium; ears small; right antihelix more prominent than the left; complexion sallow; superfluous hair on face; skin free from eruptions; mucous membranes moist and pale; tongue coated, eroded on tip; gums inflamed; pyorrhea alveolaris marked; breath foul; appetite poor; bowels regular. Heart normal in outline; slight presystolic murmur over apex. Protruded tongue showed slight tremor; pupils equal, reacted promptly to light and accommodation; knee-jerks exaggerated, right greater than the left; plantars diminished; anesthesias over the whole surface of the body, including the face; she showed no reaction to deep pin-pricks, although to some extent this may have been due to the mental dulness. She could not recognize heat or cold when applied to the surface of the body, nor was she able to distinguish the gustatory tests used—salt, sour, sweet, or bitter; called a solution of quinine when placed on her tongue, sour; unable to recognize any of the olfactory tests; said pepper-

mint was bitter, cloves didn't know; called stench hartshorn; astereognosis present; grip, right hand 14 kgs.; left hand, 9½ kgs.; coarse tremor of extended hands; gait unsteady and uncertain; balancing power impaired, involuntary evacuations of the bladder and bowels; urinalysis negative; no sugar, albumin, or casts.

Wassermann reaction with the blood serum and the cerebrospinal fluid negative. Cerebrospinal fluid clear; protein content not increased; Noguchi test negative. Cell count 1 per c.mm. Differential: lymphocytes, 98 per cent.; large mononuclears, 2 per cent.

The notes made for the next three days showed that mentally the patient was dull and apathetic; responded promptly to all questions, but was able to give little additional information in regard to personal matters; gave name of the country in which she was born, but could not give the name of the county or parish. Her replies were irrelevant and accompanied by outbursts of laughter. This tendency to laughter was also shown when she heard the voices of anyone around her or whenever anyone approached the bed. She had a mistaken identity of all persons in her environment, although she recognized her aunt on her visits. She appeared clearer so far as she was able to comprehend and carry out some simple orders given, although there was a retardation and some incoördination in all her movements. When asked where she was she said she was at home, but that she had just been down the river on a boat with President Taft and his daughter Helen. At this time she carrried out the following orders after considerable hesitation: right forefinger on left ear; right hand on left knee; left hand on right knee.

The neurologic symptoms above mentioned still continued; deep reflexes all exaggerated. At this time there was present on both sides a wrist clonus, also a slight Babinski; anesthesias were still present, but there was an area on the inner side of the right thigh, just above the knee, about the size of a silver dollar, which showed a delayed reaction to pin-pricks.

The following is an abstract of the clinical notes for the next ten days, December 15 to 25:

Consciousness still clouded. She gave prompt replies to all questions, but still showed a tendency to confabulate; on one occasion said she had just returned from the Bureau of Engraving and Printing; that she was employed there, and again that she had been at her home. As a rule all replies were incorrect. Said she was born in Ireland, but when asked the county said first County Limerick and then County Mayo, when in fact she was born in County Clare. Still had a mistaken identity of persons, and showed uncontrollable laughter. Whenever she heard anyone speaking near her she laughed heartily without cause. She continued to have incontinence of urine and feces. At this time she was able to

comprehend and carry out simple orders as follows: Right forefinger on left ear; right heel on left knee; left heel on right knee; all movements were unsteady and ataxic. Romberg present; gait unsteady; marked Babinski. All deep reflexes were still exaggerated; there was marked clonus of both wrists and ankles on both sides. Anesthesias were not so marked; she was able to recognize deep pin-pricks on almost all parts of the body, but could not localize light pin-pricks.

During the next five days the patient showed some improvement. She had learned the names of two physicians, the head nurse, and two noisy patients in the ward, but was unable to identify them. She was disoriented to place and time. She was at this time able to give the names of one or two of her employers, the name of the church she attended in the city, the correct county and parish in Ireland in which she was born, and gave correctly the names of her relatives in this city and in Ireland. Falsification of memory continued: Said she was at the Y. M. C. A., and had just returned from the city.

The deep reflexes continued exaggerated; ankle clonus and wrist clonus present; also Babinski; anesthesias were not so prominent as formerly; patient responded to light pin-pricks on face, hands, and inner side of her legs and thighs.

During the next five days, December 30 to January 5, patient continued to improve, especially on the physical side. She appeared to be able to comprehend all instructions without much effort on her part so that she was able to coöperate. When told to put her right forefinger on her left ear she put her right forefinger on the right ear. When asked if that was correct she said, "No, you said my left ear." She then placed her left forefinger on her left ear. When asked to extend her right hand she extended her left hand. When told to extend her right and left foot she did so correctly. After five minutes these orders were again repeated, and this time she failed in all. She still showed some impairment of the sterognostic sense; she recognized a number of objects placed in her hands, but failed in several others. The physical examination at this time showed sordes of the teeth and tongue, mild gingivitis. Patient was hyperalgesic to pin-pricks of the face and ears, the nipples, sacral region, and soles of the feet. After much experimenting she recognized light touches of cotton wisps. Thermic sense appeared normal over the entire body; gustatory sense normal; olfactory: said camphor was smelling salt; stench, pleasant. Equality of grip, 10 kgs. each. Reflexes: triceps and radials and ulnars markedly exaggerated. Knee-kick exaggerated, with slight clonus; plantar and tendo Achillis present; no defense reaction from the feet; jaw-jerk present; abdominal absent; Babinski on both sides; slight Romberg present; gait ataxic; eyelids on closure and extended hands showed tremor; tongue deviated to the right

side. Five days later this patient was up and dressed; was able to feed herself and had sphincter control; said she was living in the Capitol Building; that she had been living there five years; said she was not insane, but had a weakened mind from taking gas.

For the next ten days, up to January 20, patient improved both physically and mentally; showed orientation, but was unable to recall any of the occurrences in her life for the past two months; assisted with work about the wards. She could recall all the principal events of her own life up to the time of the accident, but showed an anterograde amnesia for subsequent occurrences.

From this time on the patient improved rapidly; regained insight and reacted normally to her environment. A mental examination at this time, about February 1, showed that she had recovered her mental faculties, but there was an anterograde amnesia covering a period of three months.

As she was in poor physical health she was retained in the hospital until April 7, when she was discharged as recovered. The physical examination on that date showed the following results: Patient recognizes pin-pricks and light touches all over the body; thermic and stereognostic senses normal; olfactory and gustatory senses normal; no Romberg present; pupils respond sluggishly to light and accommodation; sympathetic scarcely visible; right and left triceps very active and exaggerated; radial and ulnar present; right knee-kick exaggerated; tendo Achillis diminished; plantar reflexes very slight; no defense reaction. Patient did very well in giving the above tests. She was willing to coöperate; her actions were inhibited.

If one seeks analogous cases of psychic disturbances from carbon-monoxide poisoning in the literature very few will be found. What strikes the attention most forcibly when the cases are compared with each other is that almost every case has its own stamp and each one presents a clinical picture different from the others. Le Dosseur has collected a number of cases in which the following mental disturbances followed: aphasia; acute delirium; transitory chronic delirium; mental confusion; amnesia; melancholia; dementia. On the physical side he found muscular paralyses of diverse types; hemiplegias; paraplegias and monoplegias; various trophic disorders; convulsions, etc.

The mental condition of this patient on first observation was deep confusion. She answered questions readily as one in advanced stages of senility is apt to do. All answers were accompanied by silly laughter and none were correct. However, the examination of the patient during the first few days showed that dementia was only apparent, and that there was a lack of power of attention and concentration which prevented intelligent conversation and made her replies unreliable and incorrect and the product of her own imagination.

The principal manifestation of psychic disturbance in these cases is a loss of memory. The amnesia produced by oxide of carbon poisoning is generally sudden in its appearance and not slow and progressive like traumatic or alcoholic amnesia; it is a characteristic symptom appearing suddenly and extinguishing at once the entire past, and reducing to almost nothing the perception of the present surroundings. It may be the only apparent symptom in a mild case of poisoning and soon disappears, or it may be accompanied with disturbances of attention. The amnesia may simulate the Korsakoff syndrome in the polyneuritic psychosis with confabulation, pseudo-reminiscences, etc. A defective memory may exist in a certain number of cases which recover. This amnesia is retrograde or anterograde in type; it is variable in course and intensity; in some cases it is transitory, lasting often only a few hours or days; in others it persists for months or years; or it may be continuous, and again it may require the use of memory exercises to produce any results. In this patient it lasted nearly three months, blotting out this period from her life. More than one month elapsed from the time of the accident until the mental symptoms developed, or at least were recognized, and her admission to the hospital. We are unable to determine from information received how much her memory was impaired after the acute effect of the poisoning had run its course. If there was a defect present it was not apparent to her friends and relatives with whom she came into daily contact. When she began to regain consciousness in the hospital she had a complete retrograde amnesia. After several weeks she showed anterograde amnesia only, that is from the time of the accident and subsequent thereto. The patient was able to recall the details of her life the day before the accident, but she could not recall any of the events occurring from the time she fell asleep in her surroundings on the evening of November 2 until the middle of the month of February, when under treatment in this hospital. After her recovery the total periods of amnesia were three months.

Sachs, who has compiled a treatise concerning these complications, says: "In the early stage of convalescence a total amnesia is especially typical, either extending over the time before the poisoning, retrograde, or to the things of the present, anterograde. The falsifications of memory which were noted in this case during the first month show the Korsakoff syndrome. Stierlin reports this symptom in two of his patients. In the records of these cases one finds the various forms of amnesia diversely associated. Le Dosseur cites Brourdel's case of a physician, who following an incomplete intoxication, lost his memory totally. Arriving at his patient's house he forgot her name and the course of the illness in her case. The amnesia lasted eighteen months, at the end of which time he fully recovered. Le Dosseur mentions in his study

a lithographer who was amnesic to such a point that he was obliged to consult an indicating board in order to recall the colors that should be applied to each part of the plate. M. Bricard reports a case of a decided retrograde amnesia. A woman, aged twenty-one years, attempted suicide. The amnesia was complete in all that related to the suicide. She knows it because she was told of it, but doubted very much. As to events immediately preceding the suicide there was found a retrograde amnesia for at least one week.

Many writers call attention in this intoxication to a marked aphasia, although sometimes it is mentioned as a simple trouble of speech in the form of an embarrassment or stuttering. This apparently is not a true aphasia, but may rather be designated an amnesic aphasia, since with the disappearance of the amnesia the aphasia becomes less marked or disappears altogether.

Sometimes in coming out of the coma there appears an acute transitory delirium which may last a few hours, accompanied by excitement in which the patient is euphoric to a degree. This delirium is rarely accompanied by hallucinations, but in chronic intoxications the delirium is more prolonged, and is accompanied by various hallucinatory disturbances, which may take the form of delusions of persecution. At this stage our patient did not show delirious experiences of any description.

Kraepelin observed that when those affected first awake from the sleep of the poisoning in many instances there is an interval free from any disturbances which lasts days or weeks, and then suddenly or gradually the severe symptoms of the disease manifest themselves, and some relapses are recorded. In this connection Weidner says: "It is not possible to separate the after phenomena from the acute symptoms in a sharp manner, for in most cases the source of the same extends back to the acute stages with the exception of a few phenomena of special brain affections which appear after a free interval, or become manifest after such interval; and secondly, the boundary between the disturbances which must be ascribed to the acute poisoning and those which are to be understood as after phenomena are so labile that up to the present there appears to be no unity of opinion concerning them."

The case under discussion showed such a reaction to the effects of the intoxication, for after the acute symptoms had subsided she was well enough to be about her usual duties for at least ten days or two weeks before the mental symptoms became evident. Abrahamson cites a similar case in which a patient of his was comatose for two days following an acute intoxication from illuminating gas, when her intelligence returned and she went home. Two weeks later she developed a psychosis.

A marked reduction in the emotional field has been observed by many writers. Recently Pfeifer has described singular phenomena

which often attracts attention in poisoning from coal gas; that is, the fixed mask-like expression of the face. The emotional tone of this patient for nearly two months was one of indifference. There were abrupt outbrusts of an irresistible tendency to laughter. These outbreaks were spasmodic in character, and occurred without provocation. All her replies were accompanied by causeless laughter and it was evident whenever anyone approached her bed. This emotion had no depth, as she laughed when a patient in the adjoining bed was weeping. In the intervals between these attacks of laughter her face was apathetic. This appears to be a common symptom in carbon-monoxide poisoning, and has been referred to by several observers. Some of these cases show changeable humors, for they rapidly change from despondency to laughter. Stierlin mentions lack of emotion in his study. One of his patients evinced this symptom, showing a lack of proper feeling toward his sweetheart, to whom he was engaged before the accident, and expected to marry shortly. To some extent this may be explained from the characteristic autopsy results which have been reported in a series of cases where the symmetrical centres of softening were in or about the vicinity of the optic thalmus, most frequently in the globus pallidus and the lenticular nucleus, and hence in those sections of the brain which are supposed to control mimicry.

A subnormal temperature is characteristic of the first stages of the poisoning, after which it rises rapidly, attaining the maximum the first twelve hours. No record of a subnormal temperature in this case was made. The first recorded temperature, 101°, was the maximum on the first day following the trauma. On the four subsequent days it fluctuated between this and normal, and from then remained stationary. Ravine cites a case of a high temperature being reported in a child, aged eight years, which reached 110° in eight hours, accompanied by a pulse rate of 120 per minute. The pulse rate of this patient was in relative proportion to the temperature.

On the physical side we found involuntary evacuation of the bowels and bladder, exaggerated tendon reflexes, with clonus, including the Babinski reflex. We also had disturbances of sensation, including anesthesias, hyperalgesias, etc. The involuntary evacuation of the bowels and bladder existed for about one month in this hospital, and a few days prior to that. This was probably due in some degree to the mental confusion, and not wholly to the loss of spinal-cord control, for after the confusion disappeared she gradually recovered this control. It is difficult to state whether the neurologic disturbances were due to central or peripheral changes in the nervous system. However, the disturbances of sensation including anesthesias, etc., were to some extent due to the neuritis which always accompanies intoxications of this class.

Opinions differ in regard to the action of carbon monoxide on

the human economy. Haldane has shown by experiments that all symptoms, immediate and secondary, can be referred to the want of oxygen, and that they vary according to the saturation of hemoglobin with the carbon-monoxide gas. He states that "With 20 per cent. saturation the only symptom is a slight tendency to dizziness and shortness of breath on exertion. As the saturation increases, however, the symptom of want of oxygen becomes more and more pronounced, until at 50 per cent. saturation it is scarcely possible to stand, and even slight exertion causes temporary loss of consciousness." In the fatal cases 80 per cent. of the hemoglobin is saturated with carbon monoxide. However, Le Dosseur sums up his conclusions as follows: "That in cases of survival, oxycarbon intoxication leaves frequently after it a series of complications bearing principally on the nervous system. The paralysis comes from cerebral and medullar lesions, or is due to the polyneuritis, or two other causes may come into play, traumatism and hysteria. The mental troubles are sometimes connected with material alterations in the brain, hemorrhages, thromboses, softenings. Sometimes they are completely independent. In all these cases the simple anoxhemia of the red corpuscles is insufficient for explaining all the manifestations. Hysteria itself, though possible in certain cases, is unable to explain the phenomena observed. That experiments would tend to prove that carbon monoxide is dissolved in the serum and has a direct specific localized effect on the nerve cell." Mott is of the opinion that all the nervous symptoms can be explained by the thrombotic occlusions and hemorrhages which occur as the result of carbon-monoxide poisoning. These hemorrhagic conditions are more noticeable in the white matter of the brain, but this can be explained by the anatomical construction of the bloodvessels supplying these parts.

Unfortunately all observations of the course of such carbon-monoxide psychoses over a period of years is entirely wanting. Sachs in the preparation of his treatise on this subject was impressed by this fact, and states, "It would be interesting to know the further course of such cases." It is only in a mild uncomplicated case of this sort that we can make any regular comparisons as to its termination, as so many factors are to be considered. The majority of these cases prove fatal, and where this is not the case the mental symptoms vary from dementia to complete recovery. There are many things to be considered in the course and prognosis of the disease—namely, the general make-up and predisposition of the patient, the degree of poisoning, and in mine accidents we have to consider, in addition to the intoxication, the emotional stress, the overexertion and deprivations from lack of food and the exposure accompanying the trauma. Stierlin in his work gives a full report of observations made by himself and others among twenty-one survivors in the mine catastrophe at Caurrieres, on March 10, 1906, which claimed 1100

victims. These observations are of importance from the fact that they were continued over a period of two and a half years in the natural environments of the patients where they showed their psychopathologic conditions in the eccentricities of their lives and in their personal relations toward their families and friends. None of these patients made a complete recovery, although some of them were able to earn a living. The chronic effects of the intoxication, however, remained, which was shown by the neurologic changes as well as in the various forms of dementia present. He classified the mental phenomena into four groups, as follows, although none of them could be considered an entity, as each class encroached upon the other: (1) Psychoses caused by carbon-monoxide intoxication; (2) psychoneuroses caused by carbon-monoxide intoxication; (3) emotion psychoses; (4) traumatic neuroses of mixed etiology.

Mott calls attention to the fact that, considering the effect of carbon-monoxide poisoning being followed by mania, melancholia, confusion, and other mental symptoms, it must not be lost sight of that many cases to begin with are suicidal, and therefore if not actually insane at the time probably possess an insane or neuropathic temperament. This case was a pure and simple intoxication uncomplicated by any other neurologic factor. There was no inherited predisposition, nor was there present any deviation from the normal in her mental state previous to the trauma. She gave no evidence of emotional instability, had an even temperament, and was intelligent for one of her class. I am satisfied from the history given by her aunt and one of the servants who had been her friend for a number of years that suicide did not enter into this case. She was in an unusually happy mood previous to the poisoning, and besides this she was a devout Christian and always faithful in the performance of her religious duties. While the active mental symptoms abated in March she was not discharged until one month later, as her physical health was rather poor. Two months afterward she sailed to her brother's home in Ireland, where she has remained ever since. Inquiries made from her aunt show that the patient has written regularly to her relatives in this country, and there is no evidence from the content of her letters that she has undergone any change since she left. However, if the patient returns to this country the writer will endeavor to keep her under observation for some time.

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ACUTE POLYMYOSITIS.

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The following observations were made upon a microörganism obtained by blood culture in this laboratory, upon a case of acute polymyositis, in the service of Dr. Charles K. Mills, in the University Hospital. The case itself will be put on record later.

A. G.; acute polymyositis. Material at hand consisted of scrapings and exuded serum from a papular skin eruption. Save for Micrococcus epidermitis albus in the scrapings, these were sterile. Two days later a blood culture was taken (3 c.c. blood to 200 c.c. +1 per cent. glucose bouillon). Specimens were again taken from the then rapidly drying cutaneous eruption, with the same result as above. From the blood culture a coccus was obtained corresponding to the one described by Martinotti[1] in a kidney abscess and named by him Micrococcus polymyositis. The organism in the fifth generation was agglutinated quite promptly, by the patient's serum. This coccus is in many ways identical with Micrococcus pyogenes albus and aureus, and for purposes of comparison a recently isolated strain of the latter was run through with the "polymyositis" organism from this case. The technical work is appended, and from it we conclude that the organism in question does not deserve a separate species name, the proper course being to speak of it as Micrococcus pyogenes var. polymyositis.

Biologically the culture which we shall call No. 5308 in this report differs from the usual forms of Micrococcus pyogenes only as follows: Upon plates and slants both of agar and gelatin it grows as a grayish-blue colony, and only in older cultures may one see a faint grayish-yellow color. It is never dense white or bluish-white. Liquefaction of gelatin is not so rapid in 5308 as in the Micrococcus pyogenes. No constant difference, such as in

[1] Zentralblatt f. Bakteriologie, etc., 1898, xxiii, 877.

stratiform or infundibuliform liquefaction, could be noted. Upon potato there is neither the intense orange of the "aureus" nor the porcelain appearance of the "albus." The medium is not colored. On milk the coagulation does not appear completed until the third or fourth day, after which the clot is so firmly contracted that a suggestion of digestion arises. This last, however, does not occur. It seems worthy of note that no growth was to be seen in the blood bouillon flasks until the end of the third day. These differences were observed in the third and tenth generations. The Micrococcus aureus used for comparison was also tried with the patient's serum. It was lightly agglutinated in the same time as a firm agglutination was observed with 5308.

The Micrococcus aureus and 5308 gave almost identical results when injected intraperitoneally into guinea-pigs.

In rabbits a subcutaneous injection of Micrococcus aureus gave a sharply outlined local abscess. Injections of 5308 produced a diffuse, boggy, tender swelling, with a slight reddening of the skin, all of which subsided in three days without rupture or general involvement.

Both cultures under consideration were injected into the circulation of rabbits, using a completely emulsified twenty-four hour agar growth. The height of the symptoms in the 5308 animal was apparently reached at the end of the second day, and on the third morning both were chloroformed. Martinotti describes a peculiar lameness and gait, and emphasizes the extreme sensitiveness of the animal. Both our animals on the second day were huddled down in the corner of the cage and refused to move, crying piteously if they were forced to do so. No particular differences could be noted other than the greater sickness of the Micrococcus aureus animal. Intravenous injections of Micrococcus aureus gave pyemia, with numerous sharply outlined muscular abscesses very irregularly distributed, abscesses of the lungs, heart muscle, liver, kidney, and a mild seropurulent peritonitis. Injections of 5308 intravenously resulted in a few abscesses in the liver and kidney, and a very slight early plastic peritonitis. In the muscles of the extremities, along the vertebræ and in the pectorals, there were found enormous numbers of minute diffuse, pale gray areas surrounded by a zone of hemorrhage and edema of varying width. In the other muscles these were less numerous. The lesions are more severe in the Micrococcus aureus animal, and while this may suggest a lower virulence of 5308, there is surely some degree of specificity or predilection for the musculature. The virulence of 5308 is less than that outlined by Martinotti for his culture.

Unfortunately for the continuance of the work no rabbits were available when these animals were killed, and when a week later we could obtain the animals the 5308 culture had lost its virulence entirely and would not infect them. Indeed, 5 c.c. were required to kill a small guinea-pig, and it did not seem worth while to sacrifice

animals further, since no increase was noted after two passages. It seems sufficiently proved that this 5308 is one of the Micrococcus pyogenes group, and should not be designated by a separate species name.

In a recent communication Schmitz[2] closely corroborates the above findings. There are a few noteworthy differences, however. His culture produced an intensely yellow growth especially upon ascites agar. My culture, now about nine months old, gave more pigment, a delicate yellow, upon serum agar than upon plain medium; at no time was the color intense. The virulence of his culture rapidly declined upon cultivation, and he noted a decline in virulence for rabbits in a re-isolation of the coccus from an abscess upon a guinea-pig isolated subcutaneously. He could, however, raise the virulence for rabbits by repeatedly inoculating them. His culture gave an infection picture close to that of Martinotti, but his control with Micrococcus aureus failed to show muscular involvement. Mayesima[3] reports a case in which he isolated a Micrococcus pyogenes albus from the blood. He believes the infection atrium may be the tonsil.

This blood-culture finding is interesting from two standpoints: (1) It is another case to support the view that acute polymyositis is a bacteremia due to a micrococcus, with curious and rather uniform predilection for the musculature by which a subspecies or variety of a pus former can produce a definite clinical picture, with lesions more or less characteristic, and quite different from those produced by the most conspicuous member of the group to which it belongs. What determines the bacterium in its behavior is of course wholly unknown, and there is nothing in the clinical knowledge to help us. The infection atrium and the receptivity of the host probably play parts. It is suggested that the infection assumes the form of polymyositis when a Micrococcus pyogenes bacteremia occurs in a person whose condition favors rheumatism. There is of course no pathologic basis for this, as the lesions are different. F. Gottstein[4] however, reports a case which was closely associated with one of acute articular rheumatism. Some attention is being given by the writer to the infections, particularly the subacute, in which pathogenic mutations are noted, and this case is but an example.

[2] Zentralbl. f. Bakt. u. Par., Original, Band 65, 259.
[3] Deutsch. Zeitsch. f. Chir., 1910.
[4] Deutsch. Arch. f. klin. Med., August, 1907.

CLINICAL IMPORTANCE OF REFLEX PHENOMENA IN INTRATHORACIC DISEASES, NERVOUS MECHANISM, AND DIAGNOSTIC LIMITATIONS OF REGIONAL MUSCLE CHANGES IN PULMONARY TUBERCULOSIS.

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In a recent communication[1] an historical *resume* of the literature relating to the sensory, motor, sympathetic, and reflex phenomena resulting from intrathoracic conditions was given. It was shown that both rigidity as well as degeneration of the muscles over the neck and thorax had been discussed by various authors prior to the time of Dr. F. M. Pottenger's announcement (1909). Balint, in 1903, and Jessen, in 1905, gave considerable data upon both these phenomena in connection with pulmonary tuberculosis. Balint particularly noted the rigidity, Jessen the atrophy of the trapezius. Remak reported rigidity of shoulder and arm muscles on the basis of reflex tonus from the inflamed lung. Musser, West, and others have noted the increased tension in the intercostals over an inflamed lung or pleura. Rigidity of the abdominal muscles as well as abdominal pain as a sign of intrathoracic inflammation has been observed by a great many authors, and is a matter of common knowledge. The myoidema, once regarded as a diagnostic sign of pulmonary tuberculosis, is to be regarded as a symptom only of atrophy, from what cause it gives us no information. Therefore we can state that muscle rigidity and degeneration in intrathoracic conditions is not a new discovery, but has been touched upon from time to time by many observers. That as a clinical sign of intrathoracic affections it is an entity cannot be denied. There are some clinicians who fail to perceive it, for them it does not exist, but there is no question but that careful palpation will demonstrate changes in muscular tension and "feel" in every case of pulmonary tuberculosis.

Cyriax, of London, also makes a claim to priorty on the basis of statements made in *The Elements of Kellgren's Manual Treatment* in 1903. He stated, "Reflex contrations of the intercostal muscles result from many morbid conditions of the lungs, bronchi, and pleura." From what has been said such observations, however, were made prior to his writing.

I do not therefore regard these signs in the light of a recent discovery, but only a systematic exploitation of a clinical phe-

[1] J. L. Pomeroy, M.D., Critical Review of the Theory of Regional Muscle Rigidity and Degeneration in Intrathoracic Conditions, etc., Interstate Med. Jour., September, 1912.

nomenon which has been previously rather unsystematically studied.

In regard to the sensory phenomena in this disease, here too there have been many observations. Pain in diseases of the chest has long been recognized, and the earlier authorities thought it always due to pleurisy *per se*. Intercostal neuralgia was early recognized. Louis (1843) and Günsberg (1856) also described a hyperesthesia over the skin and muscles in the neck and back in pulmonary tuberculosis. Schmidt, in 1899, described various symptoms on the part of the sensory and sympathetic nervous system. He describes a neuralgic tenderness over the brachial plexus in apical tuberculosis, and noted paresthesias about the chest and arms, with hyperhidrosis and other disturbances. Many observers have reported evidences of peripheral neuritis, pains in the legs, arms, thighs, and other parts of the body (Beau, Leudet, and others). Pitres and Vaillard, in 1898, and Hammer, in 1899, investigated the question of peripheral neuritis in pulmonary tuberculosis, and found that there were three types: (1) Latent neuritis with no symptoms but neuritis demonstrated post mortem; (2) neuritis with sensory symptoms only; (3) neuritis with motor and sensory symptoms. In my own experience these disturbances are quite common, and at times troublesome to treat.

From a pathologic standpoint, while many authorities are conservative as to the neuritis being a specific result of the tubercle toxin, the weight of opinion is in favor of its being so. De Renzi observed degenerative changes in the phrenic nerve 27 times out of 29 cases; Jappa, Oppenheim, Steinert, Siemmerling, Cestan, and others have demonstrated degenerative changes in the peripheral nerves. Many other workers have confirmed these findings, and it seems to be proved that the tubercle toxin causes degenerative changes in the peripheral nervous system and in some instances even in the cells of the cord itself. Furthermore, irritative symptoms on the part of the toxin upon the brain and the meninges without actual tubercle formation have been observed. In some instances a mild meningo-encephalitis (not tubercle formation) was to be demonstrated. While in some instances the symptoms seem to rest upon the basis of a pure functional disturbance, probably due to cachexia and defective nutrition, the occurrence of neuritis in subjects where these factors did not exist is proof that they are not necessary causative agents.

The influence of alcohol, lead, syphilis, etc., is a difficult question to decide. While it must be admitted in certain cases that they do play a factor particularly predisposing, here again they are not necessary factors. I have seen a true Korsakoff (polyneuritic psychosis) and other neuritic symptoms in pulmonary tuberculosis where these factors were absent.

In regard to the phrenic, intercostals, vagus, and other nerve

fibers in the thorax, there is to be mentioned the effects of mechanical disturbance. Certainly the brachial plexus, the vagus recurrens (bronchial gland enlargement), and other nerves are involved in adhesions, etc., which cause deficient nerve function and peripheral and reflex phenomena.

Therefore it is to be concluded that while there is need for more definite anatomical research upon this question, it seems certain that pulmonary tuberculosis may cause definite degenerative changes in the nervous system; neuritis, posterior root inflammation, meningo-encephalitis, and other changes not due to tubercle formation, and further, these changes result not infrequently.

From the standpoint of reflex phenomena considerable work has been done. Prior to the time of the appearance of Head's classical schemata only desultory reports are to be found. Herpes zoster in pulmonary tuberculosis was frequently commented upon (Rendu, 1894, and others). Among the many reflex phenomena observed was pseudorheumatism of the shoulders (Bozzolo, Laserre), painful points about the apex and back (Schmidt, 1899), pain and tenderness in the intrascapular region, and over the second to seventh dorsal vertebræ (Petruschky, 1903, et alius), referred pain to the hypogastrium in diaphragmatic pleurisy (Günsberg, 1856, and Rosenbach, 1887). Sensitiveness to pressure and superficial hyperesthesia were noted by Walshe in 1860. Lange, in 1871, also described the referred pain to the epigastrium in diaphragmatic pleurisy. Cornet, in 1899, also mentions hyperalgesia over the affected area.

Furthermore, Würtzen, in 1906, gave an exhaustive review of the literature upon reflex hyperalgesia and pulmonary tuberculosis. His article and Schmidt's, in 1899, and the monograph of Jessen, in 1905, enable one to follow the literature almost to the present, and give vast sources of information. Francke, in 1908, demonstrated the close connection between the limits of the lesion by deep hyperalgesia, pressing the fingers deeply into the superficial tissues. Würtzen used only light touch with a blunt instrument, and showed close connection between the lung involvement and the hyperesthesia. He felt that this phenomena rested on the segmental theory of visceral reflex disturbance according to Head's zones. Head's zones were worked out on the basis of numerous cases of herpes zoster, and show the segmental areas upon the skin surface for pain, heat, cold, and trophic disturbances, and on the basis of various visceral diseases certain maxima are to be found in the skin. These zones are so well known that further elucidation is unnecessary. White and Van Norman recently have brought out a reflex hyperalgesia in the skin over the diseased lung, which limits itself only to the area involved. They give no mention of Würtzen, yet they have practically repeated his work. Wheaton, in 1910, claims to have demonstrated integument atrophy over the diseased area.

Head's reflex areas in connection with lung tuberculosis represent mainly the third to the fourth cervical zones, and the third to the ninth dorsal zones. When lower zones are stimulated he finds also the gastric factor in play, which would stimulate the same zones. Reflex disturbances also occur in connection with the fifth cranial nerve, with headache and tenderness. Jessen, Eggar, Goldman, also have studied this problem.

On the basis of these segmental studies it has been demonstrated that in pulmonary tuberculosis, one may find certain maximum points, often at the apex over the trapezius, between the shoulder-blades, tenderness over the vertebræ (frequently the second, third, and fourth dorsal), hyperalgesia over the second rib just inside the shoulder-joint area, points over the anterior part of the chest according to the seat of the lesion, also hyperalgesia of the skin proper, delimiting the diseased area, a deep hyperalgesia (Francke), an atrophic condition of the skin, sensitive areas over the abdomen (referred from the lower dorsal segments), and finally there may be referred disturbance in the region supplied by the fifth nerve over the head and face.

It is to be seen therefore that there are several factors in the problem of muscle change in intrathoracic lesions. The influence of the tubercle toxin on the peripheral nervous system, the mechanical influence in the thorax upon the nerves, and, furthermore, the reflex disturbances according to the segmental law of Head's zones. Recently, Harris brings forth a so-called diagnostic tender spot over the insertion of the levator anguli scapulæ in pulmonary tuberculosis. One may find many such tender points about the chest in intrathoracic disease, whether from tuberculosis or other conditions, and this sign is only a part of the complexes referred to, hyperalgesia. Alone such a tender point is of no diagnostic value in pulmonary tuberculosis.

Probably the most common areas of tenderness observed in connection with apical tuberculosis are over the middle of the trapezius ridge, over the brachial plexus area, the third and fourth dorsal vertebræ, and anteriorly over the second intercostal space near the sternum, and also to the inner side of the shoulder-joint on the chest. Where the disease affects the lower lobes we find tenderness over the fourth, fifth, sixth, and lower vertebræ, a tender spot at the lower angle of the scapula, in the axilla, and over the lower dorsal zones on the anterior part of the chest, and onto the abdomen. Often the points which show tenderness may be covered by a pin-head; again they are larger. They may indeed be bilateral in some instances. Between the shoulders over the rhomboidei and the levator scapulæ one not infrequently observes tenderness. A remarkable fact is that one observes these tender areas often at the earliest and again long after the patient is apparently well. In many instances there are no subjective symptoms

whatever, and their existence is unsuspected; again a dull boring ache may be complained of. Head states that the area of the second dorsal zone is commonly affected. Also the sixth dorsal segment. The two main points of this area are situated the one posteriorly at the level of the seventh dorsal spine, just internal to the angle of the scapula, and the other in front and under the breast. The lower area or the lowest two areas of the cervical plexus are also frequently affected. To these areas belong the tender points at the posterior aspect of the shoulder-joint, and those over the second rib and under the clavicle. Also the inner side of the arm and axilla.

When one considers the motor phenomena in pulmonary tuberculosis there comes into consideration the following: paralysis of the vagus recurrens; paraplegia; phrenic nerve paralysis; polyneuritis; changes in the distribution of the ulnar, peroneus, crural, and other nerves. Senator describes an interstitial myositis (gastrocnemius), with paraplegia. Balint noted changed electric reaction in the chest muscles over the affected lung; myoidema (Stokes, Tait, and others) was long held as a sign of pulmonary tuberculosis. Contractions and irritability and weakness of the orbicularis, the masseter, the sternocleido mastoid (Bozzolo), and atrophy of the trapezius over the affected area have been noted. Weakness of the voice is a common symptom. Several instances of phrenic nerve paralysis have been reported. (Vierordt, Rosenheim.)

Pottenger systematized the muscular phenomena and claims that by light-touch palpation one can pick out the diseased area in the lung by the condition of the overlying muscle tissue with a fair degree of accuracy. In early lesions the neck muscles, the trapezius, and muscles covering the apex are more rigid than normal. In late cases they become flabby and degenerated.

In regard to the atrophy of the trapezius, as described by Jessen, he considered that a local toxic diffusion in the muscles overlying the diseased lung only hypothetical, and with no substantial evidence to support it. He considered a latent neuritis to be a more plausible cause, and further felt that there might be some connection between the muscle atrophy and the segmental reflex phenomena after Head's theories. Pottenger believes that the muscle spasm results from the reflex excitation of the segments by afferent stimuli from the lung through the sympathetic nervous system to the cord, and their exciting neighboring centres in the anterior horns, with consequent spasm, as occurs in appendicitis, etc. Thus he explains the rigidity on the basis of Head's zones for visceral reflexes. The degeneration, he believed, was due mainly to overwork. I am inclined, however, to believe it to be of a trophic nature, from disturbance in the nervous mechanism in the spinal cord or in the nerve endings. Niehans in commenting

on the atrophy of the muscles about a tuberculous focus in bone tissue inclines to the toxic theory. The close segmental relation, however, between the nerves supplying the joint and the muscles moving the same would in my opinion be in favor of some nerve disorder of trophic nature.

In regard to the effects of the tuberculous toxin upon the muscles in pulmonary tuberculosis, Phillip regards the process as a progressive muscular dystrophy, in which all the muscles, somatic as well as visceral (heart, etc.), partake.

From the standpoint of trophic influence being the cause, particularly of the localized atrophy over the lung lesions, the findings of Gibson are of importance. Gibson (1911) agrees with Head and MacKenzie in regard to the segmental disturbances in angina pectoris, and further found, with Eichhorst, that in the painful areas, wasting of the muscles and changes in the texture of the skin, with increased myotatic, galvanic, and faradic irritability, were to be demonstrated. These observations distinctly support the theory that reflex disturbance of the cord through the sympathetics from the lungs will cause atrophy in the muscles corresponding to the segments affected.

When we come to consider the numerous sympathetic disturbances in pulmonary tuberculosis the theory of a nerve disturbance for the basis of muscle atrophy and rigidity gains more weight. Inequality of the pupils; flushing of the face, often unilateral; localized sweating (in hands, etc.); cardiac rapidity; pigmentation of the face and breasts; loss of hair; secretory disturbances; localized edemas in the skin, etc., and numerous other symptoms, all show the effect of the tubercle toxin on the sympathetic centres. The close relation existing anatomically between the inferior cervical ganglion and the pleura and the distribution of the sympathetic fibers from the anterior and posterior pulmonary plexuses show in part the pathway of these disturbances. Therefore, I believe there is sufficient ground to show that the disturbing stimuli pass through the sympathetic nervous system to the spinal cord (at least in part) and thus disturb the anterior horn cells, both as to muscle spasm, sensory phenomena, and subsequent atrophic changes due to trophic influence.

Furthermore, the sympathetic system has wide connections with the vagus, and this in turn secures a common origin with the ninth and eleventh nerves. A reflex disturbance therefore from the vagus can stimulate the muscles supplied by the ninth and eleventh nerves. The rigidity is particularly noticeable in the two muscles supplied by the spinal accessory, the sternomastoid, and the trapezius. Therefore, these muscles may be stimulated through central connections by the vagi or through the sympathetic connections wtih the spinal cord. The dilatation of the pupil, etc., show us that these centres in the cord are irritated, and it is only

carrying the process a step forward to conclude that the motor centres are also set into heightened activity.

Again, the recent work of Karsner demonstrates conclusively that vasomotor fibers exist in lung tissue about the pulmonary arterioles.

Another pathway for referred stimulation comes from the phrenic. This nerve has been shown to be frequently the seat of neuritis, and by its anatomical relations with the pleura is open to mechanical insult. Through its origin in the third and fourth cervical segments the muscles supplied by this segment are thrown into spasm (see these muscles in segmental charts). Capp's recent work further shows that the lower intercostals also enter into the supply of the diaphragmatic pleura, and through these, referred symptoms, muscle spasm and hyperalgesia over the areas corresponding to these nerves (in the posterior part of the thorax and the muscles of the abdomen also), may result. Head and others have long claimed that pleurisy does not cause referred or segmental disturbances. Capp's work, however, casts some doubt upon this. Pleurisy certainly must play some factor in the production of muscle spasm, and I believe that it does. The close anatomical relations of the pleura at the apex with the brachial plexus, the first intercostals, and the lateral intercostals also give rise to neuralgia, neuritis, referred pain, and other symptoms along the arm, the distribution of the ulnar nerve (elbow pain), and, according to Abrams, muscular spasm is a frequent accompaniment of intercostal neuralgia. Therefore, I believe that pleurisy does at times, according to its peculiar location, not only set up localized spasm but may give referred spasm over the abdomen and elsewhere. Certainly, disturbance of the diaphragmatic pleura gives tender points over the trapezius and muscle spasm in the area supplied by the third and fourth dorsal segments.

Schmidt's researches in regard to the apex of the lung and disturbance of the brachial plexus show that here also we may have a pathway for reflex disturbance. In pneumonia and pericarditis we also note referred symptoms over the lower intercostals onto the abdomen. The differentiation of intercostal neuralgia, neuritis, and pleurisy can only be made by considering the peculiar nature of the hyperalgesia and other symptoms which are characteristic of each, Nevertheless, Abrams reports cases where intercostal neuralgia simulates visceral disease, and advises freezing the nerve at its central origin in order to differentiate the nature of the lesion. In central disturbance the pain and spasm will not disappear, but in peripheral disturbance it will.

The communications of the two upper intercostals, and the intercostohumeral nerve explain the pseudo-angina or referred pain to the inner side of the arm so frequently seen in pulmonary tuberculosis. The deficient action of the diaphragm also may

be explained on the basis of irritation either of the lower intercostals involved in pleural lesions or direct insult to the phrenic at the apex or in the mediastinum.

The thoracic sympathetic system which joins the vagus to supply the lungs gives off branches from its upper ganglia to the spinal-root ganglia which supply the skin over the thorax. Through these fibers therefore we have a reflex pathway to the spinal cord for the production of hyperesthesia, hyperalgesia, and muscle spasm as well as trophic symptoms. The reflexes demonstrated by Abrams, brought about by percussing the vertebræ, or by irritation of the skin causing lung contraction or dilatation and similar phenomena in regard to the heart and aorta, support the view that we have definite reflex pathways for the intrathoracic viscera.

On the conception of the constriction of the chest in cardiac disease (angina), as brought out by Mackenzie, we may state that in pulmonary disease a persistent irritation of the sympathetic nerve conduces to the irritation of the spinal segment where the fibers for the lung connect with the spinal cord. Irritation of the sensory part of the cord conduces to sensation, which is projected into the periphery innervated by the nerves of the spinal segments. After this manner the motor and vasomotor symptoms are of like segmental character. We further know that counterirritation by a blister, etc., will reduce inflammation in the lung (Brunton). The occurrence of vertebral tenderness in early cases over the second or third dorsal vertebræ show the segments that are early disturbed. The lung receives its sympathetic fibers from the third and fourth cervical segments and from the third to the ninth dorsal segments (Head). From clinical studies the appearance of tenderness over the vertebræ, tender points over the anterior and posterior aspect of the chest, with skin hyperalgesia, we can state positively that proof of the irritation of the segments from the lung is conclusive. The sensory symptoms are only a part of a complex.

In affections of the lower lobes of the lung the lower dorsal areas are stimulated, and we obtain tenderness over the seventh, eighth, ninth, and tenth dorsal vertebræ, dull pain in the intrascapular area, and tender points in the axillæ, at the inferior angle of the scapula, and also anteriorly over the chest, and often on the abdomen. In some cases with these signs very little may be found on physical examination, the patient may consider that he has pleurisy, but no friction sounds will be heard. The *x*-rays will often show a high diaphragm and adhesions between the costal and diaphragmatic pleural surfaces with enlarged bronchial glands. These phenomena are much more commonly found than is recognized by the profession.

In many cases where gastric symptoms supervene one gets the

vertebral tenderness over the lower dorsal vertebræ and hyperalgesia in the corresponding segmental areas.

When we come now to consider the diagnostic importance of muscle spasm and degeneration, together with the concomitant symptoms, certain difficulties present themselves. This arises from the complex mechanism in the causation of these various symptoms. There may be neuritis, latent or manifest, with symptoms similar to intercostal neuralgia, or disturbances in the periphery also, the neurotic condition of the patient often exaggerates the picture. Also in a mechanical way symptoms may be produced by adhesions in the pleura, with various nerves, at the apex or in the mediastinum; and finally, we have the pure segmental disturbances. It is to be remembered that the heart, aorta, and bronchial glands may give rise to segmental reflexes similar to pulmonary lesions, and also in simple bronchitis reflex disturbances occur. According to some authorities emphysema and chronic bronchitis also are factors. Bronchial gland enlargement is more common than suspected, particularly in adults.

Differences in muscular development, occupation, posture, deformities of the spine, the condition of the superficial tissues of the chest (fat, etc.), age, nutrition, as well as certain diseases giving rise to muscular changes in the neck and thorax, all confuse the diagnostic importance of muscle spasm and degeneration in intrathoracic conditions. Spondylitis, Potts' disease, paralysis agitans, torticollis, rheumatic arthritis, disease of the middle ear, brachial neuritis, cervical rib, circumflex neuritis, aortic aneurysm are a few of the conditions which may give rise to reflex changes in the muscles over the thorax and neck, which are more or less permanent and will confuse the examiner.

Residuals from former conditions leave their impression upon the tissues of the chest. Pleuritis, pneumonia, asthma, bronchitis, pericarditis, etc., alter the mechanism of the respiration and the nervous and muscular actions.

Hence, muscle spasm and degeneration, as well as the sensory symptoms of intrathoracic disease to be used as a diagnostic aid in pulmonary tuberculosis, must be interpreted with extreme care. One must differentiate between cutaneous tenderness or hyperesthesia due to pleurisy, local neuritis, and hyperalgesia due to visceral disease and intercostal neuralgia. Reflexes from distant organs are also to be considered.

Marked destruction of lung destroys the nerve endings, and reflex symptoms may be absent. While the muscle spasm gives information as to the acuteness of the lesion or its activity, and degeneration, the age and chronicity of the disease, one cannot accurately localize the lesion in the lung on the basis of these signs. They will give a relative idea of its extent, but my autopsy findings show that it is inaccurate.

Consequently, it is only a rough and inaccurate index that inflammation is present in lung tissue or intrathoracic tissue. While White and Van Norman state that, according to their experience, the reflex hyperalgesia limited itself over the diseased lung tissue, in my observation, in comparison with autopsy findings in cases upon which I had studied the reflex hyperalgesia and muscle changes, these signs give only a hint as to the intensity of the inflammation and not the extent. In other words, the muscle spasm and degeneration as well as reflex hyperalgesia were observable in a limiting way, only over the intensely changed tissue, and did not clearly show the full extent of the lesion. From the very nature of the variations in the pathologic deposits in lung tissue the bizarre changes in anatomical relations occurring in advanced cases one could not expect from signs relating to nerve tissue, and reflex in character, to give accurate delimiting information. Therefore, the conclusion must be given that reflex hyperalgesia and muscle phenomena are only general in character, and any attempt to deduct information leading to accurate localization or limitation would be illogical and by practical experience, with autopsy comparisons, proved to be uncertain and misleading. Accordingly, one must consider these signs from the standpoint of an aid in clinical examination for localizing the lesion in the lung or thorax as of variable significance.

From the standpoint of the opinion of various authors who have written upon this sign the following extracts are given:

Hart claims that the conditions observed are not due to reflex causation, but result from overwork, as described by Freund and his followers. (See Pottenger's recent review.) He also raises the question of local toxic action, but discards it as being too selective.

Bonninger claims to have demonstrated a unilateral lymph stasis which causes the tissues to be firmer than normal. He rejects the reflex theory, and believes that disease of the underlying pleura was the cause.

Orzag confirms Pottenger's findings, but regards Balint's electric reactions over the diseased area as of more significance for diagnosis. He did not consider that the muscle spasm was of any value for early diagnosis.

Wolff-Eisner compared the muscle findings with the conjunctival tuberculin reaction, and concluded that the great practical worth of light touch palpation in the recognition of muscle change was "in the recognition of the initial active tuberculous process," and hence was of value from a therapeutic standpoint in pointing out the presence of active processes.

Bredow expressed doubt as to the value of muscle rigidity as described by Pottenger. He examined 107 cases of pulmonary tuberculosis and found only 7 in which the sign was present. Against

these 7 he was able to oppose 7 others which had the same rigidity, but in which careful examination elicited no indication of any lung disease. He concludes that the sign has no value in the diagnosis of tuberculosis. He also concluded: "That the symptom of muscular rigidity as an early symptom of disease of the lung cannot be confirmed. Differences in the state of contraction and consistency of the muscles of the thorax often occur. They are to be explained as a result of painful irritation, which necessitates holding one part of the thorax quiet, or as the effect of habit and occupation on the position of the upper dorsal vertebræ and on the structure of the upper thoracic aperture." I shall not attempt to enter into a discussion of these extracts, as Pottenger has discussed them in a recent communication.

Reflex muscle rigidity and degeneration as a sign of pulmonary tuberculosis is an interesting and important phenomenon, and when studied carefully in relation to the individual conditions gives considerable information regarding the stage of the inflammation. Its use requires close study and painstaking examination, and one unfamiliar with the technique will require long practice to obtain results. The reflex hyperalgesia, the tender points over the chest and vertebræ are also of interest and part of the general segmental disturbance. Careful examination will show their frequency.

It must be remarked that a careful estimation of the bearing of sensory and motor phenomena, particularly the referred type, is of importance from the standpoint of differential diagnosis. An understanding of the referred signs of intrathoracic inflammatory conditions, particularly pulmonary tuberculosis, in pneumonia and diaphragmatic pleurisy may clear up a doubtful case.

Abrams reports a case of intercostal neuralgia simulating tuberculosis and also a pleurisy simulating appendicitis.

Sahli states: "I have even seen gastro-enterostomy performed in cases of pulmonary tuberculosis on account of gastric symptoms and the appendix removed, because of radiating pleuritic pain without the trouble having been taken to examine the patients thoroughly." "Difficile est satiram non scribere" (Tuberculin Treatment, page 83). Therefore, a study of these reflex phenomena is of importance from a differential diagnostic standpoint, and will well repay investigation.

In regard to the sensory phenomena in connection with the diagnosis of pulmonary tuberculosis, the patient's subjective sensations are not to be lightly regarded. In many instances, pain, dull ache, feeling of heaviness, or other symptoms may be felt over an area, with little to be demonstrated on physical examination; yet later developments or the *x*-rays will reveal infiltration. Dunn, Minor, and Goodall have remarked upon the truth of these observations, and they must be borne in mind. Patients may

complain of more pain on the side where the pleura is least affected (Stanton). Again, one may find the pleura completely obliterated in subjects who have never had pain. We know that pleural adhesions occur in 99 per cent. of cases (at autopsy) always thicker over the apices and upper lobes. These variations in subjective sensations are important.

The fact is that subjective sensations occasionally precede the actual physical signs, and in this degree are important.

In the use of the muscle signs as well as the reflex sensory disturbances it is well to keep in mind the following statistics: According to J. Walsh, in 3144 cases the primary lesion was at the top of the right lung, the secondary lesion usually on the opposite side, and frequently more extensive. Barnes states of 860 patients admitted to the Rhode Island Sanatorium, 72.5 per cent had lesions in both lungs, of whom 56.6 per cent, were open. Hence, from the general history of the disease we would expect to find signs of the disease in most cases in both lungs.

In conclusion, it may be stated that various reflex phenomena occur in pulmonary tuberculosis, and muscle spasm and degeneration over the chest and neck are part of a complex which results mainly from a segmental disturbance through the thoracic sympathetic ganglia to the cord; but also irritation of the phrenics, the vagus, the brachial plexus, and the intercostals as well, unquestionably are factors in the presentation of the clinical picture. A localized neuritis from the tubercle toxin is also a possibility, while an actual diffussion of toxin in the area over the inflamed lung can only be surmised. There seems to be some definite relation between the diseased lung area and the muscle changes as well as the sensory electric reaction and trophic phenomena; the rigidity indicates activity of a recent nature, while regional degeneration indicates chronicity or destructive changes. Apparently no explanation seems more justifiable than that of a segmental disturbance after Head's generalizations. The frequency and constancy of disturbance in sensation, etc., over the chest and nervously connected tissues in intrathoracic disease seems to have been but little recognized by the general profession.

A search of the literature, however, reveals that a number of authors have studied these phenomena, and it remained for Pottenger to systematically study the motor reflexes, which he has ably done. From the standpoint of the early diagnosis of intrathoracic affections, particularly pulmonary tuberculosis, from the fact that these phenomena are by no means uncommon, and possess interesting variations, the study of the sensory and motor reflexes from the chest recommends itself.

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REVIEWS

A Text-book of Practical Therapeutics, with Especial Reference to the Application of Remedial Measures to Diseases and their Employment upon a Rational Basis. By Hobart Amory Hare, M.D., B.Sc., Professor of Therapeutics and Materia Medica in the Jefferson Medical College of Philadelphia; Physician to the Jefferson Medical College Hospital; One-time Clinical Professor of Diseases of Children in the University of Pennsylvania, etc. Fourteenth edition; pp. 984; 139 illustrations. Philadelphia and New York: Lea & Febiger, 1912.

When in less than twenty-two years a book reaches its fourteenth edition, there is little need for the reviewer to attest its value. Such a record furnishes the most gratifying proof of the popularity and enthusiasm with which Hare's *Practical Therapeutics* has for years been received by the medical profession. This new fourteenth edition, however, merits comment because it has actually been thoroughly revised and largely rewritten, so that it presents the treatment of disease in accordance with the most modern teaching.

In the general make-up, the new edition is not unlike the earlier ones, the book being divided into four parts. Part I takes up general therapeutical considerations. Part II deals with drugs which are arranged alphabetically; under each drug is given its occurrence, its physiological action, its therapeutic uses and toxicology, and its preparation. Part III is particularly valuable, since it covers all the important remedial measures other than drugs, such as antitoxin, hyperemia, cold and heat, hydrotherapy, exercise, climate, diet, etc. Part IV is devoted to the treatment of disease; important diseases and symptoms being arranged alphabetically, and under each the most approved methods of treatment are given.

Of late years much noteworthy experimental work has been done upon the pharmacodynamics of many drugs. It is gratifying, therefore, to note that in this edition the accounts of the physiological action of the important drugs has been revised in accordance with the latest observations. This is especially true of digitalis, caffeine, and alcohol. Notable additions to the text are also the section on Bier's treatment by artificial hyperemia,

the use of tuberculin, vaccine therapy in general and the principles upon which it is based, and the employment of salvarsan.

Over a quarter of a century of continuous activity as clinician, investigator, and medical teacher has enabled the author to appreciate with unusual clearness the needs of the practitioner. As a consequence, in the present edition of his book, Hare has so skilfully correlated the results of laboratory investigations with clinical observations that we know of no other book in which the relationship between the scientific and practical aspects of therapeutics is made so clear or to which the physician at the bedside may turn with greater assurance of finding the help which he seeks. G. M. P.

MANUAL OF HUMAN EMBRYOLOGY. By Fifteen Writers. Edited by FRANZ KEIBEL, Professor in the University of Freiburg, and FRANKLIN P. MALL, Professor of Anatomy in the Johns Hopkins University, Baltimore. Volume II. Pp. 1032; 658 illustrations. Philadelphia and London: J. B. Lippincott Company, 1912.

AN important stage in the progress of the science of human embryology is marked off by the appearance of Keibel and Mall's work, the second volume of which is now before us. The attitude of one of the editors (Professor Mall) toward his subject is thus expressed in a recent article. "Gross anatomy as a science is bankrupt. It is made solvent through embryology which alone illuminates it." And, again, "a great field opens to us for the study of histogenesis which binds embryology to histology, to make the foundation for scientific anatomy." When such is the enthusiastic point of view, the result cannot fail to be a notable production. The work is complete in two volumes and has appeared at the same time in an English and a German edition. It is also international in character in the personnel of the contributors, for of these six are European and nine are American. The first volume was published in 1910 and the present one in 1912. The plan of the work is on the "Handbuch" type, inasmuch as small subdivisions of the subject are treated by different authors, each of whom has special knowledge of the field of which he writes.

The present volume contains seven chapters numbered XIV to XX. The development of the nervous system (Chapter XIV) is considered under the four headings: (1) histogenesis of nervous tissue; (2) development of central nervous system; (3) of peripheral nervous system, and (4) of sympathetic nervous system. Chapter XV treats of the chromaffin organs and the suprarenal body, of which only the medulla is formed of chromaffin tissue. This tissue is described as secreting a substance which produces contraction of the non-striped musculature, and especially serves to maintain

blood pressure and vascular tonus at corresponding levels. The largest of the separate chromaffin organs are the aortic bodies (of Zuckerhandl), which measure in the newborn child, 11.6 mm. on the right side and 8.8 mm. on the left side. They are situated laterally to the aorta, near its point of bifurcation. Their size becomes less in post-fetal life but they do not actually disappear. Chapter XVI describes the development of the sense organs and Chapter XVII the digestive tract and the organs of respiration. In Chapter XVIII, are included the blood, the vascular system, and the spleen. Professor Minot, in his description of blood, considers that red and white blood corpuscles have the same origin, or in other words, arise monophyletically, and in this he is in agreement with a number of recent investigators. The primitive cells from which all are derived he terms "mesameboids," and some of the descendants of these continue throughout life to have the same embryonic character, and so to serve as the source of the new blood cells. Since they can move freely they can alter their distribution in the body. At one period of fetal life they are in the liver and lymphoid organs, but finally, they migrate into the marrow of bones, and thenceforth this serves as the permanent site of blood formation. He adds, however, that this view is not secure beyond all doubt. All leukocytes, accordingly, have a unitary origin also, and Minot thinks that they develop from the primitive mesameboids, but admits that investigators are divided on this point. The other view is that free wandering cells (leukoblasts) arise directly from mesenchymal cells. Four principal classes of leukocytes are recognized: I. Young forms without granules (lymphocytes); II. older forms with granules—(*a*) finely granular (neutrophile of Ehrlich); (*b*) coarsely granular (eosinophile of Ehrlich); (*c*) degenerating (basophile of Ehrlich). Of these the finely granular leukocytes represent the chief developmental series of the white corpuscles. The blood vascular system by Dr. H. M. Evans, is based, for the most part, on the beautiful series of injected specimens of young embryos, which he has himself prepared. In the consideration of the lymphatic system, Professor Sabin clearly defends her view that the lymphatic system arises from veins, and that the lymphatics grow out by the sprouting of the endothelium of preceding vessels. In Chapter XIX there is a comprehensive account of the urinogenital organs, and the final chapter is devoted to a short account of the interdependence of the various developmental processes.

Throughout the authors have presented the results of numerous investigators with careful judgment, and these have been verified and supplemented by much original work. The result is a repositary of knowledge on human embryology, which must be of the greatest value to every student of the science, and which will undoubtedly serve as the starting point for many new researches.

W. H. F. A.

COMMON DISORDERS AND DISEASES OF CHILDHOOD. By GEORGE FREDERIC STILL, M.A., M.D. (Cantab.), F.R.C.P. (Lond.). Pp. 813, illustrated. Oxford University Press, 1912.

THE second edition of a book so highly successful needs but little comment. As the author states in the preface to the first edition, the book is no systematic treatise, but deals mainly with the everyday and the commonplace. Nothing, however, is lost by this method of treatment and much is gained; each subject discussed is treated as an entity and there is none of the inconvenience of unimportant detail. In the present edition several new subjects have been added, among which may be mentioned enlarged tonsils and adenoid hypertrophy, epilepsy, asthma, and hydrocephalus; while the sections on infantile paralysis and congenital syphilis have been rewritten.

Of the new sections, that on enlarged tonsils and adenoid hypertrophy is admirable and thorough. Not only is the importance of these conditions fully emphasized, but many facts not usually thought of in this connection are mentioned. The author is conservative as to operative treatment, but insists on thorough removal when operation is advised. The chapter on asthma is not so happy, but does properly emphasize the danger of resulting emphysema in chronic cases which is often neglected in works on diseases of children. Of the old chapters those on rheumatism and on jaundice in children stand out among many as especially helpful, and in them, as indeed in the whole book, the reader feels the personality and experience of the author, and rather than adversely criticise the frequency of "I think" and "In my experience," one is tempted to attribute to this very fact, a part at least, of the charm and value of the book. O. H. P. P.

PSYCHANALYSIS. ITS THEORIES AND PRACTICAL APPLICATION. By A. A. BRILL, PH.B., M.D., Chief of the Neurological Department of the Bronx Hospital and Dispensary. Pp. 337. Philadelphia and London: W. B. Saunders Co., 1912.

PSYCHANALYSIS is receiving constantly more and more attention not only from the medical public but also from the laity. Therefore it is not at all surprising that one of the leading exponents of Freud's theories should bring out a book on the question. This work is a brief *resume* of Freud's ideas, each important division being treated in a chapter. Most of the material has been previously published.

To understand fully the present American view of psychanalysis it might be well to trace it from its beginning. Philadelphians,

for example, prefer to treat nervous patients with the so-called rest cure and incidentally practice psychonalysis, but the rest cure with psychanalysis by trained neurologists is quite a different matter from that practised by one who is not trained in neurological lines, and as a consequence throughout the country every medical practitioner has the idea that to cure a nervous patient all he has to do is to put him to bed, feed him up on milk and eggs, and so far as his mind is concerned—why that will take care of itself (as if a mind could take care of itself) and as a consequence what resulted? Christian Scientists. This, however, like so many things, only fills one phase of the question, for they have made the mistake that some rest curists have—they have neglected the physical, while the latter neglect the mental. Now, we are having a combination in the osteopaths, chiropaths, Bohemian thrusters, while in latter days it has become the fashion to treat all diseases either by venoms, serums, or polyglandular extracts. It is no wonder that we are still seeking for a method.

Freud himself, before he elaborated his present method, was a well trained neuropathologist and neurologist. His disciples either accept everything he states without question or attempt, as much as their limitations allow, to come as near it as possible, and the consequence is that Freudian doctrines are being practised only by a few men as they should be. In Europe the acceptation of Freudian theories has not been by any means uniform, but it has been accepted by some of the best neurologists. The basis of the whole contention is that to Freud every neuroses has a sexual origin. Some of his critics state that inasmuch as Freud practises in Vienna he is judging the entire universe by this city, which is notoriously sexual. What some of these critics should do is to live for a short time only in New York, Chicago, San Francisco, or even in Quaker Philadelphia, and then they would not accuse Vienna of having a monopoly. However that may be, in this country Freudian doctrines have been only very slowly accepted. About three years ago, in a discussion of the subject before the American Neurological Association, there was almost a universal condemnation of it, and it cannot be said that many gains have been made in its adherents since then, and perhaps 90 per cent. of neurologists condemn it without hesitation. If, therefore, 90 per cent. of neurologists condemn such a method, what can be said of the general practitioner or the internist who are even less qualified to judge Freud's doctrines. The basis of the whole thing after all is that the average physician hates to think, as would the average intelligent layman, that all neuroses have a sexual cause. The idea is so absolutely abhorent to most decent living men that with almost one voice they say, "Filth, filth, nothing but filth." Now let us try to analyze the situation calmly and see if it is all filth.

Freud's conception of the sexual is very broad, and quoting from Brill, "It is just as broad as our English word love or the Greek word 'eros,' and does not at all limit itself to the gross sexual. Moreover, it must be remembered that sexuality is more complicated than one thinks." Freud further states "that the newborn child brings with it the germs of sexual feelings, which continue to develop for some time and then succumb to a progressive suppression, which is, in turn, broken through by the proper advance of sexual development and which can be checked by individual idiosyncrasies." In other words, Freud does not mean that by the sexual you or breaking the Seventh Commandment. If, therefore, one looks at it from a broad standpoint, one is compelled to admit that the strongest passion and the strongest impulse is the sexual and that it dominates every man and every woman. Why not, therefore, admit it? Is it unusual when considering the education of a child in sexual matters, that the constant "don't do this and don't do that" which accompany the growth of an individual should sometimes cause neuroses? After all, we are a race of prudes. We do not educate our children properly. We tell them all about the breeding of cats, dogs, and horses, we teach them the dangers of typhoid fever and smallpox, but, do we teach our children anything about gonorrhea or syphilis? Why not therefore admit it at first hand that it is no wonder that the sexual, looking at it in a broad way, can cause all sorts of neuroses.

So far as abnormal sexual practices are concerned everyone knows, who knows anything about life, that the abnormal sexual is quite common in the so-called normal individual. Every doctor meets with it and there are some who think it is on the increase. However that may be, on every hand one is constantly confronted with the sexual. We find in it our theatres, dramas, divorce courts, everywhere. The conclusion, therefore, must be reached that Freud is right and the sexual in a broad sense can cause and must cause all sorts of repressed ideas and neuroses. The wonder is not that it does, but why someone has not called attention to it before. The reviewer is, however, by no means prepared to admit, as Freud does, that every neurosis has a sexual basis, but he admits willingly that a great many have this origin.

Now as to what these doctrines have done and why they are gaining favor. We have been accustomed to treat our nervous patients as a class. We give them bromides, we tell them to forget their troubles (we never tell them how, by the way), we call their troubles "only functional," as though functional diseases were so easy to get rid of, but we have not done what common sense would indicate—we have not treated patients individually. Everyone must admit that no one person is like another. No person's education is like another's, and yet we have not treated

individuals as individuals, which is what Freud does, and, therefore, in that one respect alone he has done a great deal of good. Again, take his views of dementia præcox and the different delusions, hallucinations, mannerisms, and sterotype movements that these patients have. Instead of accepting the old time idea that a patient has delusions and hallucinations because he is a case of dementia præcox, Freud states that the type of delusions and hallucinations are dependent upon the individual's previous personal history. This is nothing more than common-sense.

As for Brill's book. He states in his preface that "one cannot expect to become proficient in psychanalysis unless he has mastered at least Freud's theories of the neuroses, the interpretation of dreams, the sexual theories, the psychopathology of everyday life, and his book on wit, and last but not least, who has not a training in nervous and mental work," and then he proceeds to write a book on Freud's theoreis in 325 pages. He further states that: "These assertions are not based merely on the reading of a few scattered papers, but on about six years of hard work and almost constant occupation with the subject. For it is only through hard work and long experience that one can acquire a thorough knowledge of Freud's psychology." How can he expect, therefore, that the neurologists who instinctively oppose Freud's ideas will get anything out of such a work and what can be said of the general practitioner who knows less. Certainly, after reading such a work as this with no previous knowledge on the subject, it is no wonder that most physicians are filled with loathing that such a thing is possible. It is a pity that this work should have been published. It would have been far better if the author had produced only one of the fundamental theories at a time. Of course, the answer can be made that this has been done by the author himself in his translations as published by the *Journal of Nervous and Mental Disease*, and if so, there is hardly any need for this book, because it does not do what every book should do. It does not adequately explain the subject. One thing perhaps has been accomplished; it has called attention of the medical public to the importance of the sexual in the formation of the neuroses.

T. H. W.

FIFTH SCIENTIFIC REPORT OF THE INVESTIGATIONS OF THE IMPERIAL CANCER RESEARCH FUND. By E. F. BASHFORD, Director. Pp. 94; 13 illustrations and numerous charts. London: Taylor & Francis, 1912.

THE report consists of four papers on the experimental investigation of cancer. The first paper is by B. R. G. Russell on "The

Manifestation of Active Resistance to the Growth of Implanted Cancer," and demonstrates that the power of producing immunity appears to be a part of the parenchyma of the tumor, and that it also is influenced by the soil exhibited by the inoculated animal; simultaneous inoculation of a tumor strain that rapidly induces resistance can retard the growth of grafts from a strain which tends to grow progressively; it has also been shown that mice bearing progressively growing tumors can be immunized against re-inoculation, even although this immunity does not, as a rule, inhibit the further development of the tumor already established.

The second paper, written by Wm. H. Woglom, on "The Nature of the Immune Reaction to Transplanted Cancer in the Rat" is rather controversial in nature and supports the contention of Russell as against that of Burgess, concluding that the phenomena described by Russel as characterizing the immunity of mice to tumor implantation occur also in the case of the resistance offered by rats to the Flexner-Jobling adenocarcinoma.

The third paper, by C. da Fano, on "A Cytological Analysis of the Reaction in Animals Resistant to Implanted Carcinomata" would indicate that the polymorphonuclear leukocytes and the lymphocytes are most important in the local cell reactions of immunized animals.

The fourth paper, by S. Higuchi, "On the Immunizing Power of the Placenta, Blood, Embryonic Skin, Mammary Gland, and Spleen of Different Species against Carcinoma of the Mouse" shows that the strongest immunity is produced by homologous tissues, that killed tissues produce no immunity, and that homologous spleen can produce an immunity which reaches its height in ten to twelve days following the injection.

All the papers presented are concisely and clearly drawn up, are well illustrated by drawings and charts, show keen insight into the problems studied, and can be read with pleasure, interest, and profit even by those whose special lines of endeavor do not coincide with those of the authors. H. T. K.

DISEASES OF CHILDREN. By BENJAMIN KNOX RACHFORD, M.D., Professor of Diseases of Children, Ohio-Miami Medical College, Department of Medicine of the University of Cincinnati, Pediatrician to the Cincinnati, Good Samaritan, and Jewish Hospitals, Cincinnati. Pp. 783; 107 illustrations and 6 colored plates. New York and London: D. Appleton and Company, 1912.

THE importance of pediatrics as a special branch of medicine is being emphasized by the rapid additions to pediatric literature

of such treatises as this volume, wherein the whole subject receives thorough orthodox treatment while there is shown throughout the individual stamp of the author's personal judgment and opinion. The book is essentially practical. Pathological findi ıgs are but briefly outlined and unnecessary etiological discussions are avoided in order to afford space for an ample consideration of diagnosis and treatment. In addition to routine subjects we find a consideration of otitis media and mastoiditis, and of the common diseases of the skin.

Among the introductory chapters the section on excesisve nerve activity is particularly timely. The danger of overstimulation and forced development of the child's brain in these days of nervous instability cannot be too strongly emphasized, and the note of warning gains in value coming from one so well qualified to sound it as the author.

Of much value, also, are the chapters on treatment wherein are discussed various measures, medicinal and others, as they apply to infancy and childhood. Exception might be taken to one statement to the effect that rest in bed in acute nephritis should be insisted upon until the urine findings are normal. While this is undoubtedly sound teaching in a majority of cases, yet its strict and literal enforcement in all would prolong the rest-period to an unjustifiable length, with actual harm to the child's other functions.

The important chapters upon feeding, with a careful consideration of the relations of milk to the child's nutrition, are notably clear, practical, and sensible. No subject is more difficult to present, and much that has been written in recent years has failed to accomplish its mission because of what might be termed its technical difficulties. These the author skilfully avoids. To many pediatricians it will seem that he has accorded to condensed milk and proprietary foods a much more definite place in the dietics of infancy than they deserve. This is unfortunate, since it will furnish students and practitioners with an additional excuse for the use of these undesirable substitutes for good cow's milk.

The author's conception of the various disorders of digestion and of the organs of digestion, is conservative. He avoids the extremes of the Continental school while recognizing the value of their teaching, and refuses to relinquish the lessons of years of experience for the somewhat theoretical views promulgated within less than a decade.

In the case of appendicitis it might be objected that he somewhat overemphasizes the value of "medical treatment" and places the burden of decision "when to operate" an unduly long time upon the shoulders of the physician.

Especially able are the chapters upon tuberculosis, and the lessons which he teaches could well be learned by many who are inclined rather to the belief that their student days have passed so far as clinical medicine is concerned.

To sum up, it may be said that the book is conservative while it includes all that is worthy of acceptance; and that the great care given to diagnosis and treatment make it of particular value to the practical physician in search of enlightenment and guidance.

J. C. G.

ELEMENTARY BACTERIOLOGY AND PROTOZOÖLOGY: THE MICROBIOLOGICAL CAUSES OF THE INFECTIOUS DISEASES. By HERBERT FOX, M.D., Director of the William Pepper Laboratory of Clinical Medicine in the University of Pennsylvania. Pp. 237; 67 engravings and 5 colored plates. Philadelphia and New York: Lea & Febiger, 1912.

THE discussion of a technical subject in terms which will be intelligible to the person without technical training is always very difficult. In the task, therefore, which Dr. Fox has set before him, there are many pitfalls.

This work of 237 pages is the author's maiden effort in extended publication, his object being "to give the nurse and the beginner an idea as to the nature of microörganisms and their relation to the world's economy, especially disease." There are fifteen chapters, a glossary, and a fairly full index. The arrangement of the subjects included under the general term of microbiology is good, though in the descriptions and discussions the work occasionally shows some of the faults common to many first editions, such as involved sentences and a few typographical errors. The illustrations are good though not original. When one considers the difficulty of preventing a work of this kind from becoming too technical for the average nurse or lay person, and too general for the student or nurse, going more particularly into bacterial or protozoal work, it must be admitted that the author has for the most part steered a safe middle course. The book should certainly supplant the many elementary works on this subject now in use.

F. H. K.

X-RAY DIAGNOSIS AND TREATMENT. By W. J. S. BYTHELL, B. A. Cantab., M.D. Vict., Hon. Physician to the Ancoats Hospital, Manchester (Electrotherapeutic Department); Medical Officer to the *X*-ray Department of the Manchester Children's Hospital and the Salford Royal Hospital, and A. E. BARCLAY, M.D., Cantab., M.R.C.S., L.R.C.P., Medical Officer to the Electrical and *X*-ray Departments Manchester Royal Infirmary, etc. Pp. 147; 118 illustrations. London: Henry Frowde and Hodder and Stoughton, 1912.

THE main object of this book is to acquaint the medical practitioner with the uses of the *x*-rays in diagnosis and treatment, and

to enable him to select those cases in which *x*-ray therapy or examinations are applicable or indicated. For this reason very little attention is paid to the details of manipulation of apparatus, technique, or the phenomena of *x*-ray production which characterize those works intended to appeal especially to the specialist in Röntgenology. A few pages are devoted to a brief presentation of salient facts concerning the production of *x*-rays and descriptive of the apparatus required. Most of the book is given up to the diagnostic side of *x*-ray work, and following the chapter covering each subject, are a number of excellent reproductions from radiographs of illustrative cases. Because of the wide scope of the subject as a whole and the limited space in the book, some of the chapters have had to be very brief, from the standpoint of the Röntgenologist, at least, and especially the one dealing with the diagnosis of abdominal conditions. However, each subject is covered in such a way as to acquaint the general practitioner with practically all of the applications of *x*-ray diagnosis. The short chapter devoted to *x*-ray therapy can do little more than outline the conditions in which this therapeutic agent is applicable, or can be used to advantage. H. K. P.

DIE ENTSTEHUNG DER KURZSICHTIGKEIT. Von DR. GEORG LEVINSOHN, Privat-Dozent für Augenheilkunde an der Universität Berlin. Mit 3 Abbildungen im Text. Pp. 88. Verlag von S. Karger, Karlstrasse 15, Berlin, 1912.

FROM a critical examination of the views commonly held in regard to the cause of myopia, the author concludes that neither the accommodative act nor pressure from the external muscles in convergence or lateral movements are capable of bringing about the changes observed in myopia. Experiments with the manometer in animals' eyes and the tonometer in the human fail to show the slightest change in the tension in all positions of the eyeball. Moreover, universal experience shows that the effect of increased intraocular tension is productive of changes quite different from those observed in myopia.

The author makes an exhaustive study of the fundus changes in myopia (conus, staphyloma posticum, supertraction, etc.). Emphasis is laid on the great difficulties and even impossibility of accounting for the observed anatomical changes by any of the common hypotheses.

A really effective hypothesis which shall actually account for the genesis of myopia must be based upon some influence which comes into play during near work; and as he believes to have

demonstrated that no such power can be found in the accommodation, convergence, or the lateral movements of the eyes, but a single factor remains, and one which, strange to say, has been almost unnoticed as the determining element. This factor is represented by the bending forward of the head and trunk, a factor which, he believes, exercises a very important influence upon the lengthening of the youthful eyeball. By such bending forward of the head, the globe, which is rather securely fixed in all directions, except from before backward, becomes subject to the influence of gravity which force necessarily tends to draw the eyeball forward and drag upon its connection with the optic nerve.

To demonstrate the effect of the force of gravity in the bending forward of the trunk and head the author devised an apparatus attached to the bony entrance of the orbit. From the tracings found with this it could be readily seen that the eyeball sank downward and forward upon bending the head and trunk and that such sinking was exactly proportional to the degree of the inclination of the head. The increase in the amount of blood in and especially behind the eyeball during such forward movements of the head and trunk will also affect the position of the eye to an appreciable extent and be an accessory factor in the sinking forward of the globe.

Such, in short, is the hypothesis which Levinsohn sets up for the solution of the problem of the genesis of myopia. The fact that a new hypothesis seems necessary is sufficient evidence that this important question is still *sub judice*. Whether the new hypothesis is really the long sought for solution remains to be seen. T. B. S.

THE WASSERMANN REACTION. By JOHN W. MARCHILDON, B.S., M.D., Assistant Professor of Bacteriology, St. Louis University Medical School.

THIS new book on the Wassermann reaction by John W. Marchildon, covers in detail the methods of preparation of the various reagents and the technique of the reaction according to Wassermann's original teaching.

There are a number of errors in this technique and its interpretation, and a few confusing errors in the printing.

The book concludes with a brief but clearly written discussion of the clinical value of the Wassermann reaction in the various stages of syphilis, in parasyphilitic conditions, and in diseases other than syphilis, and the effect of the different forms of antisyphilitic treatment on the Wassermann reaction, in which are many statements of value to the clinician. J. F. L.

HANDBUCH DES GESAMTEN MEDIZINISCHEN ANWENDUNGEN DER ELEKTRIZITAT EINSCHLIESSLICH DER RÖNTGENLEHRE. Professor Dr. Med. H. BORRUTAU, Privatdozent f. Psychologie an der Universität Berlin; Professor Dr. Med. L. MANN, Privatdozent f. Nervenheilkunde an der Universität Breslau; Professor Dr. Med. M. LEVY-DORN, Leitender Arzt am Rudolph-Virchow-Krankenhause in Berlin; and Professor Dr. Med. P. KRAUSE, Direktor die medizinischen Universitätspoloklinik in Bonn. Vol. II, second half, pp. 1102; 292 illustrations. Leipzig: Werner Klinkhardt.

THIS is the second half of the second volume, and is the last of the three volumes which constitute this monumental work upon the medical uses of electricity. The previous two volumes have been reviewed in this JOURNAL. Altogether, these three volumes comprise everything in the literature on the technical and therapeutic application of electricity. It is such a work as is possible to be produced only by the Germans, and is the best work on the subject.

The first volume consists of the introductory chapters on electricity and magnetism, the physiological chemistry of the influence of electricity on the human being, theories of electrical irritation, its physiology and pathology, and a beginning description of the technique and apparatus. The second volume embraces the diagnostic points of the different forms of nervous disease which are applicable to therapeutic electrical treatment. It is practically a nervous diagnosis. The third volume, and the most important one, discusses general electric therapeutic application, and is complete in every sense. It discusses principally nervous diseases, but also includes chapters by various individuals who have made specialties of such particular subjects as the heart, rhinolaryngological diseases, the eye, ear, skin, diseases of women, joint and muscle diseases, static applications, high frequency currents, uses of electric light and heat, electrolysis, cataphoreses, galvanism and phototherapy. T. H. W.

AIDS TO OPHTHALMOLOGY. By N. B. HARMON, M.D. Pp. 216; 100 illustrations. New York: Wm. Wood & Co., 1912.

IN this work the attempt is made to cover the subject of ophthalmology in the space of two hundred pages. Any such endeavor must fall short of obtaining the desired end, and result in a work of limited usefulness. The post-graduate student, for whom the author specifically wrote this book, would, we feel, be investing his time without obtaining a just proportion of thorough information by devoting his attention to Harmon's work. B. F. B. JR.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Bence-Jones Proteinuria in Conditions Other Than Myelomatosis.—Boggs and Guthrie (*Johns Hopkins Hosp. Bull.*, 1912, xxiii, 353) have found in the literature instances of Bence-Jones proteinuria in conditions other than myelomatosis. These included a case of osteomalacia, 1 of gun-shot wound of the leg, and 3 cases of lymphatic leukemia. The only instance of metastatic bone carcinoma was a case of gastric tumor reported by Oevum. The authors report an instance in a woman with primary carcinoma of the breast and metastatic dissemination in skull, ribs, both trochanters, both ilia, and right tibia. They are struck with the fact that all the cases have one point in common—the more or less extensive involvement of the bone marrow. It is also obvious that the relation of multiple myeloma to Bence-Jones proteinuria cannot be specific. Other disease processes involving the marrow may lead to the excretion of this unusual body. The excretion of the protein seems also to bear no fixed relation to the extent or duration of the disease process, as it may occur in the urine before any demonstrable bone lesions may occur, and may disappear at a time when the lesions in the marrow are most extensive. Again, very widespread involvement of the bone marrow may occur unassociated with this type of proteinuria.

The Mechanism of the Tuberculin Reaction.—F. Meyer and K. E. F. Schmitz (*Deutsch. med. Woch.*, 1912, xxxviii, 1963) report an experimental study of the tuberculin reaction. They infected four rabbits with bovine tubercle bacilli (Perlsuchtbacillen). At varying intervals after the infection became well established, they withdrew

blood from the ear vein. Whole blood, serum, and washed corpuscles were then incubated for a short time with bovine tuberculin (Perlsucht-tuberkulin), and the mixtures, often after standing twenty-four hours in the ice chest, were injected into normal rabbits. Tuberculous serum plus tuberculin, with or without the addition of complement, may produce a febrile reaction when injected into a normal animal. The reaction is more marked when whole blood or washed corpuscles from a tuberculous animals is incubated with tuberculin and then injected intravenously into normal rabbits. Fever, dyspnea, prostration, and sudden lowering of the temperature may follow. As controls, the blood and corpuscles of normal rabbits incubated with and without tuberculin, and tuberculous blood and corpuscles incubated without tuberculin were used. Only minimal rises of temperature were observed which subsided rapidly. It was shown that the toxic substance which is formed during incubation of washed corpuscles and tuberculin may pass into the salt solution in which the corpuscles are suspended.

The Origin and Significance of Basophilic Granules in the Erythrocytes.—M. GEORGOPULOS (*Wien. klin. Woch.*, 1912, xxv, 1704) has made observations on changes in the blood following splenectomy which tend to show that basophilic granules in the erythrocytes are derived from the nucleus and are, therefore, indicative of regeneration of the blood. Two days after removal of the spleen, with red cells, 2,350,000, and hemoglobin, 44 per cent., normoblasts became very numerous in the patient's blood. Evenly distributed in the cytoplasm were numerous granules which were stained a blackish blue with Giemsa's stain. The cytoplasm of these normoblasts was orthochromatic. The granules were found only in the normoblasts—none were observed in non-nucleated cells. This fact the author points out, suggests very strongly a nuclear origin of the granules. Since the basophilic granules were present only in young cells in this instance, it is unlikely that they represent degenerative changes.

Lordotic Albuminuria and the Acidity of the Urine.—E. FRAENKEL (*Deutsch. med. Woch.*, 1912, xxviii, 1974) has examined the relationship between lordotic albuminuria and urinary acidity as determined by titration with tenth normal sodium hydrate, using phenolphthalein as indicator. In some cases the albuminuria was induced by having the patients assume the lordotic posture in a chair for fifteen minutes. In many of the children, an increase in urinary acidity occurred with the appearance of albumin in the urine or with the augmentation of a preëxisting albuminuria brought on by the lordotic position; in others, the acidity rose several hours after the albumin appeared. It was possible to suppress the albuminuria by previous administration of sodium bicarbonate, thus supporting Fisher's views. However, in a child whose condition corresponded to lordotic albuminuria following scarlatinal nephritis, as well as in scarlatinal nephritis itself, the administration of alkali was without effect.

Insect Transmission of the Virus of Poliomyelitis.—HOWARD and CLARK (*Jour. Exper. Med.*, 1912, xvi, 850) have experimented with the house fly, certain types of mosquitoes, the bedbug, and head and

body lice, with reference to their ability to carry the poliomyelitic virus. The insects were allowed to feed directly on infected cord or upon materials containing a suspension of infected cord. They were then killed at varying intervals and used whole, or in part, for the preparation of bacteria-free Berkefield filtrates, which were inoculated into monkeys. Biting insects were made to feed upon monkeys inoculated with poliomyelitic virus and their bodies used in turn for inoculation. The experiments allow these deductions: The domestic fly may become contaminated with the virus which it may obtain in nature from infected discharges from the nose and throat or intestine. The virus can be transported in a living state on the surface of their bodies for two or more days, and within the esophagus and stomach for at least several hours. The virus may be deposited at a considerable distance from the point of contamination. The flies may die, and the disintegration of their bodies may liberate surviving virus in dust. Through such a passive contaminator as the house fly, the bodies may easily be taken into the bodies of human beings. At least two species of mosquitoes are excluded. The pediculi also seem incapable of taking virus out of the blood, or maintaining it in a living state within their bodies. In one of the sixteen experiments with bedbugs, it was shown possible for a blood-sucking insect both to obtain living virus from the blood and maintain it in a living state for at least seven days.

The Bacteriology and Chemistry of the Bile in Vivo, Together with a Method for the Early Diagnosis of Typhoid Fever.—G. KIRALYFI (*Berlin. klin. Woch.*, 1912, xlix, 1985) has made bacteriological and chemical studies of the bile, with particular reference to affections of the gall-bladder. His method is practically the same as that used by Petry (1911) in an examination of the microscopic elements of the bile. The patient is given Boldyreff's oil breakfast consisting of 250 c.c. to 300 c.c. of olive oil; the stomach is, however, first washed with sterile water through a sterile tube, after which the oil is introduced through the tube. After one-half hour, the stomach contents are removed with a sterile tube. The patient is instructed to expectorate all sputum and saliva during the half hour the oil remains in the stomach; in fact, it is essential that nothing be swallowed. The stomach contents are received into a sterile dish. In a few minutes the oil separates above the bile-stained fluid, which has entered the stomach. By means of a sterile pipette, some of the fluid is transferred to tubes of agar and bouillon. The remainder of the bile-stained fluid is used for microscopic and chemical examination. The main object of the study was the bacteriology of the bile in cholecystitis. For purposes of orientation, various diseases were included. In all, 69 patients were examined. In 39 instances, the bile-stained fluid was sterile, showing that the technique employed was successful in preventing the entrance of mouth organisms. In 7 of 8 cases of cholecystitis, the author obtained positive results; the colon bacillus was found four times, the streptococcus once, and staphylococci twice. The sterile fluid was obtained from a patient whose clinical symptoms were mild. In cholelithiasis, the bile was usually sterile. This result Kiralyfi believes was due in part to mechanical interference with

the flow of bile from the gall-bladder, in part to the fact that in a certain percentage of cases gallstones are independent of bacterial invasion. In subacidity and anacidity, the gastric flora may interfere with the bacteriological examination of the bile; this difficulty is not encountered in hyperacidity or normal acidity. In 3 cases of typhoid fever, pure cultures of the Bacillus typhosus were obtained from the bile. This result was especially important, for in 2 of the patients cultures of the blood and feces were negative, and the Widal reaction also remained negative. Normal bile contains no albumin. In testing for albumin, material remaining in the stomach was excluded by the lavage, and, as a further check, the wash water was tested. The sulfosalicylic acid test was used for albumin. A positive reaction was obtained in all of the cases of cholecystitis in which bacteria were found; the two conditions run parallel. A trace of albumin (mucin, etc.) is to be disregarded. In cases where there is a strongly marked reaction for albumin with negative culture, the possibility of a latent or masked cholecystitis without symptoms must be considered. Microscopic examination of the bile is not of great value. One or two pus cells are without significance. It is only when the cells are abundant that their presence points to an inflammatory exudate. The albumin may be increased regardless of the number of pus cells.

Alimentary Galactosuria in Liver Disease.—E. Reiss and W. Jehn (*Deutsch. Archiv f. klin. Med.*, 1912, cviii, 187) find that galactose is superior to levulose in some respects as a measure of hepatic function. Galactose was first used in hepatic diagnosis by Bauer in 1908. The authors have administered 40 grams of galactose in the morning on a fasting stomach, as Bauer did, after the patient has voided urine. The sugar is best taken in a carbonated water. An hour after taking the galactose, the patient may have his breakfast. (If the patient has diarrhea or is vomiting, the test should be delayed; the authors have never seen either of these symptoms as a sequel of giving the sugar.) The urine is collected for twelve hours, in two six-hour periods. The greater part of the sugar—usually all—is eliminated in the first six hours. After twelve hours, none is excreted. The urine is tested qualitatively with Nylander's and Trommer's tests, quantitatively with the polariscope or by titration. In normal individuals and in those in whom liver disease could be excluded, 1.5 gram at most was recovered—usually none, though it must be added that one neurasthenic excreted 2.5 gram. The authors consider amounts pathological only when they exceed 2 grams. The authors have employed the test in more than 100 patients with liver disease and have found, as did Bauer, that alimentary galactosuria is unusual in many diseases of the liver. Thus, in cholelithiasis it was usually found that galactose was excreted in normal amounts. Obstruction of the bile passages by tumors never led to galactosuria. Luetic icterus (secondary stage) gave negative results in 3 cases, moderate galactosuria (2 to 4 grams) in 2 cases. Of 8 cases of chronic passive congestion, only 1 showed a moderate galactosuria. Fifteen cases of cirrhosis of the liver were studied. In the majority the tolerance for galactose was normal; in only 3 cases was a moderate galactosuria found. Among 17 cases of catarrhal jaundice, only 1 very mild case failed to show galactosuria.

The galactose was usually excreted in moderate or large amounts, as much as 36 per cent. of the quantity given being recovered. Of other conditions, only 1 case of croupous pneumonia showed galactosuria, other cases of this disease being negative. Thus, a normal tolerance for galactose speaks against catarrhal jaundice alone; it may be found in all other hepatic conditions. (The authors have had no opportunity to study acute yellow atrophy and phosphorus poisoning, but believe a galactosuria will be found in these conditions.) Similarly, in the absence of febrile disease, marked galactosuria indicates catarrhal jaundice, or possibly one of the two conditions mentioned above. Moderate galactosuria may occur in most diseases of the liver. It is lacking in cancer and is rare with cholelithiasis and chronic passive congestion.

Carcinoma Skin Reaction.—The relation of the skin reaction for carcinoma proposed by Elsberg, Neuhof, and Geist to the isohemolysin classification (Moss) has been shown not to be a matter of indifference. There appears to be one group, Group IV (the corpuscles of which are neither agglutinated nor hemolyzed by any serum in vitro) which might be utilized for the reaction with reasonable reliability, since when these corpuscles have been hemolyzed, hemolysis of those of the other three groups has always occurred. This fact demonstrated by Gorham and Lisser has led LISSER and BLOOMFIELD (*Johns Hopkins Hosp. Bull.*, 1912, xxiii, 356) to test a series of cases, making use of only the corpuscles of Group IV. They studied 62 verified cases of carcinoma and sarcoma and 94 cases of healthy individuals or patients suffering from non-malignant aliments. Two-thirds of the malignant cases gave a positive reaction. In the control cases 91.6 per cent. were negative. They concluded that a negative skin reaction adds little or no weight to the evidence against cancer. But a positive reaction is strong presumptive evidence of cancer. They believe the corpuscles of Group IV must be used to give reliable results.

Nitrogen Retention in the Blood in Experimental Acute Nephritis.—FOLIN, KARSNER, and DENIS (*Jour. Exper. Med.*, 1912, xvi, 789) following the development of colorimetric methods of nitrogen determinations in the blood, studied the possible nitrogen retention in experimentally produced nephritis. The types of nephritis selected were those produced by uranium nitrate, by potassium chromate, and by cantharidin. In the uranium nephritis, which involves both tubules and glomeruli, the former more markedly than the latter, a marked accumulation of nitrogen occurs in the blood. Chromate nephritis, involving tubules almost exclusively, results in only moderate nitrogen retention. Cantharidin causes a nephritis of both tubules and glomeruli, especially the latter, and in this type there is produced a marked early and persisting accumulation of nitrogen. It must be noticed that the glomerulus is distinctly involved in the two forms where accumulation of nitrogen in the blood is most marked, a condition indicating that although almost pure tubular involvement produces only moderate accumulation, the additional involvement of the glomerulus is extremely important in leading to a retention of nitrogenous waste products.

SURGERY

UNDER THE CHARGE OF

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Anesthesia of the Sciatic Nerve.—BABITZKI (*Zentralbl. f. Chir.*, 1913, xl, 227) says that for successful anesthetization the injection must be intraneural. Paraneural injections are extremely unreliable. In the best cases the anesthesia may be insufficient and in the worst we risk the development of general toxic symptoms before the occurrence of the anesthesia. Paraneural injections of salt solutions in large quantities, give good results in sciatica. Although much of the fluid is absorbed there still remains a considerable quantity in a compact layer pressing on the nerve. It is otherwise with a toxic anesthetizing fluid. Novocain solution (2 to 3 or even 4 per cent.) must be economically employed. Babitzki uses the following method: The finger in the rectum reaches to the point where the nerve bends over the edge of the great sciatic foramen to pass downward in the groove between the tuberosity of the ischium and great trochanter. The great sciatic foramen is formed from the great sciatic notch by the great sciatic ligament passing from the sacrum to the spine of the ischium. The spine of the ischium is easily found by the finger which is then made to press upon the bone and ligament in the whole circumference of the foramen carrying the contents of the foramen before it. The nerve is almost entirely covered by the pyriformis muscle and only a small portion of it lies below the margin of this muscle between it and the bony edge of the foramen. The injection needle is introduced, under the control of the finger in the rectum, through the gluteal muscles down to the foramen, and the needle point can be made to find any desired portion of the thick nerve trunk. It is of the greatest importance that the nerve itself can always be found. When the nerve is injected the result develops rapidly within a few minutes—not in the course of an hour or half an hour (Jassentzki and Wojno). The method has been employed in 15 cases, in which the results were completely satisfactory. It was used for amputation of the femur, Madelung's venesection, inflammatory process of the foot bones, fractures of the femur and bones of the leg, as well as for sciatica. About 5 c.c. of a 3 per cent. solution of novocain is first injected into the anterior crural nerve, by Lawen's method, when the patient is turned face downward. The fractures gave most difficulty, for which the necessary precautions must be taken. The

patient usually will have had applied first aid to the injured dressing, which should not be removed until after the injection is made. The technique and the rules of asepsis for the manipulations in the rectum are generally known.

Subcutaneous Rupture of the Diaphragm and Positive Pressure (Meltzer).—RIEBEL (*Surg. Gynec. and Obst.*, 1913, xvi, 133) made a study of the literature after an experience with a case of rupture of the diaphragm in a boy, aged ten years, who had a wagon loaded with gasoline cans pass over his left leg and side of chest, the boy lying prone on the ground. Operation showed the entire stomach in the pleural cavity and the entire left half of the diaphragm, as far back as the costal angle, detached from the ribs at right angles to its fibers. Inspection revealed the stomach and intestines as well as parenchymatous organs uninjured. A postmortem was not held. From his study Riebel concludes that the diaphragm has an important influence upon the heart's action, by its anatomical relation to the heart and pericardium. It is an important factor in the circulation by aiding the venous return, especially from the abdominal cavity. It plays an important part in maintaining equilibrium in the thoracic cavity. Rupture of the diaphragm must needs be followed by serious disturbances in respiration and in the equilibrium within the thoracic cavity. The inevitable prolapse of abdominal organs following subcutaneous rupture still increases this condition, frequently producing a state of positive pressure in the thoracic cavity. The use of differential pressure is absolutely necessary to overcome these factors. It will insure better results, in these cases, permitting, furthermore, the choice of abdominal or pleural route or both as the occasion requires. The character of pressure, whether positive or negative, is of little consequence, but the method of Meltzer is simple and can be used anywhere. In cases of suspected subcutaneous rupture of the diaphragm, insufflation should be employed with low pressure (10 to 15 mm.) before operation, to overcome the deleterious effects of disturbed intrathoracic equilibrium.

A Case of Extensive Subcutaneous Emphysema Following Intratracheal Anesthesia, with Recovery.—LUKE (*Surg. Gynec. and Obst.*, 1913, xvi, 204) reports the case of a woman, aged thirty-six years, operated on for a decompression under intratracheal insufflation, for a cerebral tumor. The patient was placed in the prone position, with the head strongly flexed over the end of the table, which proved to be a bad position for breathing and for managing the giving of the anesthetic. The color and pulse were entirely satisfactory for the first ten minutes. During the next twenty-five minutes there was a moderate cyanosis occasionally which was relieved by extending the head a little. About ten minutes later the blood in the wound was noted to be very dark and the face was cyanosed and generally swollen, especially on the left side. The intratracheal tube was withdrawn without a moment's delay and the patient quickly turned to the dorsal position and artificial respiration begun. There was also a marked swelling as far as the umbilicus, anteriorly, and to the base of the spine posteriorly, all of which gave the characteristic crackle, on palpation, of subcutaneous emphysema. The decompression operation

was performed after some improvement in the condition of the patient, under a very small amount of drop ether. The patient recovered to die from a later operation for the removal of the tumor. The following possibilities are considered in explanation of this accident: (1) That of the direct trauma due to the catheter either during introduction or afterward; again from pressure of the long narrow sand bags under the neck. (2) Trauma brought about by overdistention: Here is considered the possibility of inserting the catheter too far, and thereby plugging tightly a bronchus, leading to overdistention and rupture of the lung. In this case perhaps obstruction was possible from the extreme flexion and pressure of the sand bags beneath the neck. Again the catheter may have been too large (No. 24 was used), but from experience this seems unlikely. This is the second accident of this kind in New York City during the use of this method. The other case resulted in death and was thought to be due to the catheter slipping into a bronchus and plugging it, with consequent excessive distention and rupture of the lung. It is admitted that errors in technique may have been entirely responsible for this accident; but it teaches the valuable lesson that the method is not entirely without danger, and, further, that a safety device (which was not applied to the apparatus in either of the above cases) which will efficiently guard against high intrapulmonary pressure, is absolutely essential.

Treatment of Wounds of the Venous Sinuses of the Cranium.—Auvray (*Arch. gén. d. chir.*, 1913, lvi, 257) collected from the literature 163 cases of wounds of the superior longitudinal and lateral sinuses and reports 3 new cases. He emphasizes the gravity of the prognosis and studied the various therapeutic procedures and their comparative value. He discusses the employment of sutures, of forceps which are left in position, of the lateral and circular ligature, and of the tampon. The latter is the oldest of all and in Auvray's stastistics was employed in 75 out of 112 cases operated on. In 9 other cases the method of hemostasis was not indicated. In favor of the tampon are its simplicity, the rapidity with which it can be applied, and its great efficacy. Even when the suture or forceps pressure is employed, the tampon serves as a complimental method, and renders more perfect the hemostasis of the venous wound. The necessity of leaving the wound open exposes the patient to the danger of the introduction of infectious material and the development of phlebitis which was common in the earlier cases. But the present-day use of sterile and antiseptic gauze, as iodoform gauze, makes these complications little to be feared. Another objection raised against the tampon is the danger of pressure by it upon the brain. Auvray did not experience this complication in any of his cases, and believes that it will be of minimal importance in any case, since it can be obviated at any time by the removal of the tampon. He maintains that the superiority of the tampon over all other methods is incontestible.

THERAPEUTICS

UNDER THE CHARGE OF

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Further Observations on the Treatment of Human Cancer with Intravenous Injections of Colloidal Copper.—LOEB, LYON, MCCLURG, and SWEEK (*Interstate Med. Jour.*, 1913, xx, 9) report a further series of 19 cases of human cancer treated with repeated injections of colloidal copper. Rapidly growing tumors which lead to extensive metastases in the internal organs are not amenable to this treatment. In a large number of cases the effect of the injections gradually decrease. This method, however, causes a gradual although partial retrogression of the large majority of inoperable cancers, provided they have not reached the final stage of the disease. However, they believe that the method is too slow in its action to render probable a cure except in a few cases. They say in addition that it is too early to predict the ultimate fate of the patients who are now under treatment.

Pneumothorax Treatment of Pulmonary Tuberculosis.—V. JAGIÉ (*Wein. med. Woch.*, 1913, lxiii, 379) gives the following as necessary conditions before inducing artificial pneumothorax for therapeutic purposes: (1) Good motility of the chest wall that above all should not be adherent to the apex of the lung. Adhesions at the base do not prevent the desired compression of the diseased lung. Pain during the injection is a symptom of the presence of adhesions. (2) It is necessary that the cavity walls be thin and compressible. If the walls are fixed the method is of no use. (3) A good heart action. The author says that this therapy is especially indicated when there are a number of cavities of greater or smaller size on one side with few adhesions, and on the other side only slight infiltration or an apical lesion. The treament is also indicated in any disseminated unilateral tuberculosis. Persistent hemoptysis is also an indication when one knows the bleeding side. Jagié has also seen good results obtained in tuberculosis of the larynx where the benefit derived was probably due to its good effect upon the cough. Intestinal tuberculosis and amyloid degeneration are contraindications to the treatment. Tuberculous pleurisy is a problematical indication for the treatment. The best age for the treatment is from fifteen to thirty-five years, but this procedure can also be utilized in tuberculosis of children.

Benzol Treatment of Leukemia.—NEUMANN (*Therapie d. Gegenwart*, 1913, liv, 56) reports a case of leukemia that improved remarkably after a course of thirty-six days' treatment with benzol. He followed Koranyi's directions, giving at first one 0.5 gm. capsule of benzol twice a day and increasing the dose to two capsules of 0.5 gm. each four times a day. Soon after the end of the benzol course the patient

developed fever and diarrhea, with repeated epistaxis and hemorrhagic stomatitis and rhinitis, and died thirty-nine days after the discontinuance of the benzol. Neumann states that the bone-marrow findings resembled those found by Selling in benzol-poisoned rabbits. The benzol used is not specified by Neumann, and Selling thought that the toxic action of the benzol used in his experiments was probably due to anilin present in the benzol as an impurity. Neumann believes that benzol is a very effectual remedy for leukemia, but its use requires great caution. He thinks that it should be discontinued as soon as a distinct tendency to improvement begins.

The Emetin Treatment of Amebic Dysentery.—ALLAN (*Jour. Amer. Med. Assoc.*, 1913, lx, 664) says that for a number of years, English physicians working in India have maintained that ipecac is the best remedy for amebic dysentery, and within the past few years the American profession has largely come to agree with them. In March, 1911, Vedder, working in Manila, published his findings that a fluidextract of ipecac would kill amebæ in cultures in dilutions as high as 1 to 200,000. The next year Rogers in Calcutta found that emetin hydrochlorid killed amebæ in stools in dilutions of 1 to 100,000 and began the use of this salt hypodermically in cases of amebic dysentery. His brilliant results led Allan to try this method of treatment and he reports two cases of amebic dysentery in detail that were promptly cured by subcutaneous injections of emetin hydrochlorid.

Induced Pneumothorax in the Treatment of Pulmonary Disease.—HAMMAN and SLOAN (*Bull. Johns Hopkins Hosp.*, 1913, xxiv, 53) describe the history of the production of artificial pneumothorax for the treatment of pulmonary tuberculosis, the proper selection of cases for this treatment, the different methods, of which two are mainly in use, Brauer's method by incision down to the pleura and Forlanini's puncture method. Hamman and Sloan prefer the latter method. They give in detail their method of inducing pneumothorax. The chief dangers attending induced pneumothorax are two—infection and air embolism. Air embolism is the more important complication and has followed attempts to produce pneumothorax only upon the injection of gas in the absence of satisfactory evidence that the needle is in the pleural cavity. The whole procedure of producing and maintaining pneumothorax should be guided by the manometer, and the authors give very valuable data regarding the information given by the manometer. Hamman and Sloan's conclusions are as follows: (1) Induced pneumothorax is a harmless procedure and the operation, carefully performed, is without danger. (2) In 3 out of 20 cases it was impossible to produce any pulmonary collapse owing to general pleural adhesions. (3) Of 16 cases in which pneumothorax was successfully produced in but 7 was the pneumothorax complete. (4) Of 9 cases with induced pneumothorax existing for four months or longer, 4 have developed pleurisy with effusion. (5) The pneumothorax has, in most instances, an immediate and striking influence upon the cough and expectoration, tubercle bacilli may disappear from the sputum. (6) Constitutional symptoms abate more slowly. In most instances there is at first a loss in weight followed by a gradual

rise. (7) The total collapse of one lung causes surprisingly little inconvenience. Usually there is but slight dyspnea on exertion. Many of the patients with an induced pneumothorax assist actively in the work about the sanatorium. (8) The procedure is of great value in the treatment of pulmonary hemorrhage. (9) While induced pneumothorax will never become a routine method for the treatment of pulmonary tuberculosis, still in selected cases it offers a prospect of temporary and permanent relief when the usual methods of treatment have been unsuccessfully tried. Quiescent lesions in one lung with acute recrudescence in the other are the most favorable for the treatment. Its use need by no means be limited to strictly unilateral lesions, but when there is advanced disease of both lungs little benefit can be expected. It would seem advisable not to withhold the treatment until the patient is hopelessly advanced, but to apply it judiciously to suitable moderately advanced patients in whom the disease tends to progress in spite of appropriate treatment. The article is a valuable one and should be consulted for details of the procedure.

Experiences with Induced Pneumothorax.—Van den Bergh, de Youg and Schut (*Beiträge z. klin. d. Tuberkulose*, 1913, xxvi, 47) report 13 cases where pneumonothorax was produced for therapeutic purposes in pulmonary tuberculosis. They believe that this procedure should be restricted to cases of severe pulmonary tuberculosis when the lesion is chiefly or entirely unilateral and should be used in these cases only when the ordinary methods of treatment have failed to benefit. There is danger of increasing or making more active a slight tuberculosis of the opposite side and this danger must be taken into consideration. This result occurred in some of the cases reported, and in 2 it was confirmed by autopsy. The direct dangers of the operation, chiefly air embolism and injuries to the lung, are very slight with good technique. A marked effusion should be partly withdrawn before inducing pneumothorax or afterward, in maintaining the pneumothorax. An artificial pneumothorax should only be induced by an expert, preferably in a hospital where advantage may be taken of Röntgen-ray examinations. As to the choice of methods for producing the pneumothorax they believe that the puncture method of Forlanini should have the preference over the incision method of Brauer.

Benzol in Leukemia.—Wachtel (*Deutsch. Med. Woch.*, 1913, xxxix, 307) reports 2 cases of leukemia where he gave benzol. The first was a case of severe myeloid leukemia and he was obliged to stop the benzol after the third day, as albumin appeared in the urine. The second case showed marked improvement under 3 gm. of benzol given daily. In the first two weeks the improvement was apparent only in a return to a normal temperature and an improved general condition. In the fourth week the leukocytes dropped from 102,000 to 37,000. In the first three weeks the mononuclears predominated, but after this the myelocytes decreased and the polynuclears increased, and the spleen returned to normal size. A blood examination made four weeks after the benzol had been discontinued showed a hemoglobin percentage of 78; red blood cells, 4,200,000; white blood cells,

8,000, of which 80 per cent. were polynuclear neutrophiles, 12 per cent. lymphocytes, and 2 per cent. each of eosinophilic and neutrophilic myelocytes. The fact that the hemoglobin percentage and the number of reds increased while under the benzol treatment is especially noteworthy.

PEDIATRICS

UNDER THE CHARGE OF

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Tuberculous Infection in Children.—ARMT DE BESCHE (*Deutsch. med. Woch.*, 1913, xxxix, 452) reports an interesting investigation to determine the percentage of tuberculous infection in children. Lymphatic tissue from the mesenteric, bronchial, and cervical glands of 134 children coming to autopsy was injected into guinea-pigs and rabbits, and the results studied and followed out. In 28 of these children tuberculosis was the cause of death. In 14 it was discovered, latent at autopsy. In 10 cases only "latent bacilli" were found in the lymphatic glands. Tuberculous infection was proved in 52 of the 134 children. The percentage of infection rose proportionately with the age period, from one to fifteen years. In the greater percentage of lymphatic tuberculosis the condition was found widespread and general throughout the body. In 45 of the positive cases the bacillus was found to be of the human type, proving that the greater majority of tuberculous children receive the infection from human beings. In 3 cases the bovine type of bacillus was isolated, and 1 case showed both the human and bovine type. This investigation was made in the city of Christiania, and apparently shows that from 6 to 8 per cent. of tuberculous infection in children comes from cows and the balance from human beings.

Length of the Incubation Period in Infantile Paralysis.—CARL SCHOUG (*Deutsch. med. Woch.*, 1913, xxxix, 493) determined the average incubation period in an epidemic of anterior poliomyelitis in Sweden. He also attempted to trace the method of infection, especially in two families, closely associated, in which 6 children were afflicted. From his series of cases Schoug determines the average period of incubation to be about four days. As the infectious element exists in the blood as well as in the secretion from mucous membranes, the transmission of the disease is made possible through blood-sucking insects as well as directly or indirectly from person to person by infected secretions. In Sweden a large number of cases occur in winter, when the stinging fly is not in evidence. To accuse the fly, therefore, one would have to assume a very long incubation period. His investigations do not point to blood-sucking insects for the dissemination of the disease, nor did it seem probable that the horse-fly could have caused the

infection of such a large number of people in two families, from the original case afflicted with that disease. It seems much more likely that the infectious secretions of the nose and mouth from the original case directly or indirectly infected the other members of the families.

Effect on the Child of Salvarsan given to the Syphilitic Mother.—MARIE HOLTH (*Deutsch. med. Woch.*, 1913, xxxix, 462) reports 9 cases in which pregnant women with syphilis were given salvarsan with most beneficial effect on the subsequent condition of the children. In only 2 of these cases were there any syphilitic symptoms in the children, who were under obesrvation from ten weeks to one year after birth. The majority of these women received the treatment during pregnancy. Some had given birth during the previous two years to syphilitic infants. In 7 of the cases no syphilitic symptoms developed in the child. One woman was given the treatment while nursing a congenitally syphilitic child. Through the mother's milk the child received the benefit of the treatment also, and the syphilitic signs disappeared and it developed normally. These cases show that this treatment of the mother or the prospective mother exerts a very favorable influence on the vitality and development of the child.

The Mental Defective and Society.—WILLIAM LELAND STOWELL (*Archives of Pediatrics*, 1913, xxx, 203), after describing the condition known as defective or feeble-minded, gives the number of feeble-minded individuals in the United States as more than 300,000. In New York State there are 30,000, of which less than 4000 are in institutions. Special classes for defective children, separating the abnormal from the normal and giving them work according to their needs, is primarily approved of. The practical outcome of this fine work is criticised because a subnormal child should be in an institution all the time, not a public school a short time. Scarcely one-tenth of the children ever rise to the normal grades. All feeble-minded individuals should be segregated in public or private institutions. This applies especially to feeble-minded girls and women because of their lack of moral force. In 300 families containing mental defectives there were 2013 children born, 434 of which were defective and 160 criminal or pauper. Statistics are abundant and experience the same everywhere. In several homes for prostitutes as high as one-third were found to be feeble-minded. The possibility of procreation is the most vital factor in the large class of feeble-minded. Feeblemindedness is an incurable condition, not a disease. Out of 341 patients discharged from an institution, 85.5 per cent. were subsequently found to be absolutely useless, and should have been taken care of for life. Preventive measures in the form of sterilization for all feeble-minded not segregated should be required by law, to avoid the multiplication of this unfortunate class.

Practical Points in the Management of Breast Feeding.—ERIC PRITCHARD (*Archives of Pediatrics*, 1913, xxx, 164) deprecates the lack of attention and study given to breast feeding by pediatrists and obstetricians. He calls attention to the common mistakes made in the management of breast-feeding, especially during the first weeks

of life. First and most serious of mistakes is to give the infant the usual dose of castor oil. The meconium supplied by nature acts a an intestinal lubricant and offers sufficient stimulus to the nerve centres regulating defecation. Castor oil overstimulates these nerve centres, dislocating their automatic functions. The delicate epithelial lining of the intestinal canal is injured by the oil, which sweeps out the meconium and tears off shreds of mucous membrane. Meconium is so important to the bowel that where it is deficient Pritchard replaces it by petroleum emulsion, the best substitute known to him. It is protective, lubricant, and soothing. The incidence of thrush in infants is often due to loss of epithelium from cleansing the mouth of the infant with a clean rag to render it aseptic. Preserving the continuity of the epithelium will keep the mouth more healthy than cleansing with a linen rag. Another point of greatest importance is the management of the number of feedings. Pritchard claims better results from three- or four-hour intervals between feedings than from the usual method of two-hour intervals. This gives a long interval of rest between feedings. If the quantity of breast milk is insufficient for this long interval it should be supplemented by a feeding of appropriate food immediately after the breast. Pritchard voices a distrust of the caloric method of infant feeding. The quantity of food should be estimated by a "test feed," and if below the normal standard a supplementary feeding should be begun. A "test feed" consists of weighing an infant three hours after its last breast feeding, then putting it to the breast for a regular feeding, and weighing the child immediately afterward to determine the quantity of food taken. Infants too often do not obtain progressively larger quantities of milk as they grow older. The supply of breast milk will vary with the hygienic environment of the child. The "test feed" applied systematically shows that London children at least secure an amount of breast milk enormously below the usually accepted estimates. This suggests modifications in the method of breast feeding and of artificial feeding. An infant requires time to learn to digest a new food. New foods therefore should be given at first in very small amounts or in a predigested form.

Some Cases of Jaundice in Childhood.—F. J. Poynton (*British Jour. Child. Diseases*, 1913, x, 145) discusses several types of jaundice occurring in infancy in which diagnosis is difficult. He cited 3 cases in which the jaundice appeared during the first four days of life. These cases showed moderate jaundice, liver enlarged, but not hard, stools white and undigested, but no enlargement of the spleen. At times bile appeared slightly in the stools and the jaundice and the size of the liver diminished slightly. These cases recovered gradually in from seven to twelve months. They were never breast fed. They are clearly obstructive cases, and not of the same nature as acholuric jaundice, or icterus neonatorum. Poynton suggests an unusually viscid bile as a possible cause. The treatment and feeding of these cases is difficult. Fats are not tolerated and nutrition is diminished. Foods used successfully by Poynton include malted milk, Walker-Gordon modified milk with low fats, raw meat juice, and brandy. Among drugs the most serviceable were small doses of gray powder,

and bicarbonate and salicylate of soda. The second type of jaundice is known as congenital, family, periodic jaundice in which the disease runs in families and shows an acholuric jaundice with enlargement of the liver and spleen, and anemia of varying degree. The blood shows fragility and reticulation of the red cells. Jaundice may disappear temporarily with the development of grave anemia and a large, hard spleen. Severe recurrent pain over the spleen and epigastrium is rather characteristic. The third type of jaundice is syphilitic in origin. Three cases are reported in children, aged seven, nine, and ten years. There was a history of "fits" or epileptiform attacks in all of them. The first two cases had enlarged livers with intense jaundice and bile in the urine, and ascites. They developed chronic meningitis and succumbed. Both showed parenchymatous changes in the liver and endarteritis. The third case developed jaundice, pale stools, and enlarged liver, but on antisyphilitic treatment recovered and ultimately developed fairly well mentally and physically. The Wassermann reaction should be of assistance in diagnosticating this type.

GYNECOLOGY

UNDER THE CHARGE OF

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Nervous Sequelæ of the Artificial Menopause.—A considerable series of clinical investigations have been carried out by MOSBACHER and MEYER (*Monatschr. f. Geb. u. Gyn.*, 1913, xxxvii, 337) to determine if the nervous phenomena, which are commonly supposed to follow the artificial menopause, have a basis in demonstrable physical changes in the organism. One of their chief lines of investigation was to determine if the theories of Schickele (recently discussed in this department) with regard to the blood-pressure reducing action of the internal secretion of the ovary could be demonstrated clinically. For this purpose they have tested before and at varying periods after operation the blood pressure of 67 women who were subjected to double oöphorectomy, considering a rise or fall to have taken place only when the readings varied by 10 mm. or more —Sahli instruments. They found after operation a rise in 13 and a fall in 17 cases; in 7 of the former and in 9 of the latter marked nervous disturbances were present; in the other patients these were lacking. Mosbacher and Meyer conclude, therefore, that the blood pressure cannot be considered in any way dependent upon the presence or absence of ovarian secretion, nor can the occurrence of nervous phenomena be considered a result of blood-pressure changes; they have thus been entirely unable to confirm clinically Schickele's physiological experiments, or to demonstrate such an antagonism between the ovarian and adrenal secretions as he believed to exist. Tests directed to ascertaining

whether any increased stimulation of the sympathetic nervous system occurs after castration, as evidenced by a change in the amount of adrenalin necessary to produce glycosuria when introduced subcutaneously, or of cocaine to produce mydriasis when dropped into the eye in very weak solution, produced likewise totally inconstant results, from which no definite conclusions could be drawn. As a result of these investigations, and of clinical observations in general, Mosbacher and Meyer express themselves as being extremely skeptical with regard to the existence of any causal relation whatever between operative castration and the occurrence of definite nervous disturbances, believeing that most of these which do occur, apparently as a result of operation, are in reality manifestations of psychoneuroses which have little or nothing to do with removal of the ovaries. In substantiation of this contention they quote a few instances of women, upon whom no operation had been performed, and whose internal genitalia were entirely normal, but who presented to a marked degree all the typical symptoms usually ascribed to the artificial menopause. They also found that a considerable number of patients complaining after oöphorectomy of hot flashes, attacks of sweating, palpitation of the heart, etc., had also been troubled with the same conditions before operation, whereas in other cases symptoms of this nature which had existed before operation disappeared after it. With regard to the occurrence of postoperative disturbances of a more psychic nature, such as mental depression, anxiety, irritability, Mosbacher and Meyer claim that all patients complaining of these admitted the presence of "nervousness" beforehand, entirely new symptoms occurring only in very occasional instances.

Acute Tuberculosis following Gynecological Operations.—A number of quite remarkable cases are reported by PROCHOWNIK (*Zentralbl. f. Gyn.*, 1913, xxxvii, 7) to illustrate the possibility of the occurrence of rapidly spreading acute tuberculosis, leading to a fatal termination, in individuals in whom there was not the slightest suspicion of a tuberculous infection, the immediate causative factor in most of these being some apparently trivial operative procedure. The salient features of the most instructive of these cases are, very briefly, as follows: (1) Curettement for dysmenorrhea and irregular bleeding. Entirely well up to the ninth day, then suddenly high, remittent fever. Lungs and pleura free until ten days before death, which occurred in a very few weeks. Autopsy: Miliary tuberculosis arising from uterus and right tube; tubercles over entire peritoneum; fresh miliary foci in lungs and pleura. (2) Reposition of retrodisplaced uterus (narcosis). Well up to seventh day, then high, remittent fever. Death in eleventh week. Autopsy: general abdominal tuberculosis; moderate involvement of lungs and pleura. Origin, a tuberculous focus in right tube, which had been torn loose from the rectum by the forced reposition of the uterus. (3) Forced reposition of a retrodisplaced uterus by means of the sound (narcosis). Following this, a parametric abscess formed, which was opened and drained. Wound healed, but high, remittent fever came on, and lasted for four and one-half months; lung involvement only in last two weeks. Autopsy: acute miliary tuberculosis in abdomen; fresh foci in lungs; origin

from right tube. (4) Abortion (self-induced), curettement; death on forty-eighth day. Autopsy: tuberculosis of both tubes, miliary tuberculosis of entire peritoneum; small, recent foci in lungs and pleura. (5) Double salpingectomy for gonorrheal pyosalpinx (gonococci demonstrated in the pus). Death on the forty-ninth day. Autopsy: extensive peritoneal tuberculosis; no involvement of lungs; few tubercles in pleura. In none of these women was there the slightest reason to suspect the presence of a tuberculous focus anywhere, except that the husband of one was known to be tuberculous, and in two of the others this was suspected. The patients themselves were all in good health, except for the condition for which the operation was performed, and in none did repeated examinations of the lungs by trained internists reveal any signs of trouble until shortly before the end. While Prochownik admits that cases of this sort are fortunately extremely rare—the ones reported are culled from an experience of many years—the fact that they may occasionally occur should be a warning, he thinks, to the utmost caution in dealing with all cases in which there is even the possibility of a tuberculous infection of the genital tract, since they prove the fallaciousness of Krönig's commonly accepted dictum, to the effect that "genital tuberculosis leads extremely rarely to miliary tuberculosis, and practically never causes, either directly or indirectly, the death of the individual."

DERMATOLOGY

UNDER THE CHARGE OF
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Industrial Skin Diseases.—Karl Herxheimer (*Deutsch, Med. Woch.*, January 4, 1912) refers to seventy-four means through which chronic eczema may be acquired. Industrial acne, vaccinia in milkers, furuncle in workers with cement, ulcers from glass, sand, and dust, and workers in chromium salts are mentioned. Where the tarry products are used, frequent washings of the skin should be resorted to in order to prevent inflammation of the follicles and skin.

Contagious Diseases of the Skin.—J. T. Bowen (*Boston Med. and Surg. Jour.*, December 14, 1911) directs attention to the common contagious diseases of the skin of frequent occurrence in schools, referring specially to impetigo contagiosa, ringworm, marginated dermatitis of the thighs and axillæ, verrucæ, alopecia areata, and scabies. He urges supervision of the children and young persons in schools and institutions.

Etiology of Leprosy.—William Turner, of Gibraltar (*Brit. Jour. of Derm.*, September, 1911), cites the case of a man, imbecile from birth, an inmate of the Gibraltar lunatic asylum for nineteen years, at the

end of which period he first showed cutaneous lesions on hands and feet, deemed for a year to be syphilitic, but subsequently proved to be leprous. Notwithstanding the usual disfigurement and deformity attending the disease the general health for a number of years remained good. How this man became the subject of leprosy it seemed impossible to discover. No case of leprosy had been known to exist in Gibraltar for thirty years or longer, and the patient had had no communication with the outer world, except at intervals with his sisters who were healthy. A contagious origin in this case seems absolutely untenable. Heredity, insanitary conditions of life, uncleanliness, emanations from the soil, and food supply as possibilities of contagion were likewise not tenable theories. The bacilli of lepra were demonstrated in the lesions of the face. The patient subsequently died from swellings in the mouth and pharynx and exhaustion from lack of being able to partake of nourishment.

Venesection Plus Saline Infusion in Treatment of Skin Diseases.—J. SIMOND (*Deutsch. Med. Woch.*, November 30, 1911) has attained good results by this method in eczema, urticaria, pruritus, and furunculosis, and especially in cases refractory to other methods of treatment. Toxins are washed out by withdrawing 100 to 200 c.c. of blood from a vein and subsequently infusing without removing the canula 300 to 700 c.c. of a 0.9 per cent. salt solution. The operation may be repeated from 3 to 6 times every 5 or 6 days. Simond's experience extended over 100 cases of skin disease.

Salvarsan at the New York Skin and Cancer Hospital.—HOWARD FOX and W. B. TRIMBLE (*Jour. Amer. Med. Assoc.*, November 18, 1911), after eight months' experience, conclude that salvarsan is a powerful symptomatic remedy for the treatment of syphilis; that it acts with greatest rapidity on lesions of the mucous membranes, and further that it is of decided value in obstinate palmar and plantar syphilodermata. It should be used in conjunction with mercury, and cannot replace this valuable remedy, except in a few selected cases. The effect of the salvarsan on the Wassermann reaction is in general analogous to that of mercury. The intravenous and intramuscular methods of administration are probably of equal efficiency. Where rapidity of action and the comfort of the patient are to be considered the intravenous method is to be chosen.

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Lymphocytosis of Infections.

RICHARD C. CABOT, M.D., Assistant Professor of Clinical Medicine in the Harvard Medical School, Boston, Massachusetts.

Gastric Ulcer without Food Retention. A Clinical Analysis of 140 Operatively Demonstrated Cases.

FRANK SMITHIES, M.D., Gastro-enterologist to the Mayo Clinic, Rochester, Minnesota.

The Economic Aspects of Hookworm Disease in Porto Rico.

BAILEY K. ASHFORD, M.D., Sc.D., Major, Medical Corps, U. S. A.

The Serum Treatment of Purpura.

HENRY L. ELSNER, M.D., Professor of Medicine in Syracuse University, and FREDERICK A. MEADER, M.D., Assistant Professor of Bacteriology and Pathology in Syracuse University, Syracuse, New York.

Gastric Disturbances in Tabes Dorsalis.

WILLIAM FITCH CHENEY, M.D., Clinical Professor of Medicine in the Medical Department of the Leland Stanford, Jr., University, San Francisco, California.

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WILLIAM A. WHITE, M.D., Superintendent, Government Hospital for the Insane, Washington, D. C.

Value of Massage in the Treatment of Various Conditions in the Child.

JOHN PHILLIPS, M.D., Assistant Professor of Medicine in the Western Reserve University, Cleveland, Ohio.

Leukemia of Unusual Type.

LINDSAY S. MILNE, M.D., M. R. C. P. (Eng.), Professor of Medicine in the Medical Department of the University of Kansas, Rosedale, Kansas.

Topography of the Cardiac Valves as Revealed by the X-Rays.

GEORGE FETTEROLF, M.D., Sc.D., Assistant Professor of Anatomy in the University of Pennsylvania, and GEORGE WILLIAM NORRIS, A.B., M.D., Assistant Professor of Medicine in the University of Pennsylvania, Philadelphia.

Diaphragmatic Hernia, with Report of a Case.

KARL M. VOGEL, M.D., Assistant Professor of Clinical Pathology in Columbia University, New York.

The Effects of Exposure to Intense Heat on the Working Organism.

CHARLES N. FISKE, M.D., Surgeon, U. S. N.

AMONG THE IMPORTANT ORIGINAL CONTRIBUTIONS WHICH WILL APPEAR DURING THE SUCCEEDING MONTHS MAY BE QUOTED:

Acid Intoxication in Infants and Children. A Clinical Study.

ISAAC A. ABT, M.D., Professor of Pediatrics in the Northwestern University Medical School, Chicago, Illinois.

The Control of Rabies.

HENRY ALBERT, M.D., Professor of Pathology and Bacteriology in the University of Iowa, Iowa City, Iowa.

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W. L. BALLENGER, M.D., Professor of Laryngology, Rhinology and Otology in the University of Illinois, Chicago, Illinois.

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WALTER A. BASTEDO, M.D., Associate Professor of Pharmacology and Therapeutics in Columbia University, New York.

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HARLOW BROOKS, M.D., Assistant Professor of Clinical Medicine in the University and Bellevue Hospital Medical College, New York.

Congenital Dilatation of the Colon.

DAVID MURRAY COWIE, M.D., Clinical Professor of Pediatrics in the University of Michigan, Ann Arbor, Michigan.

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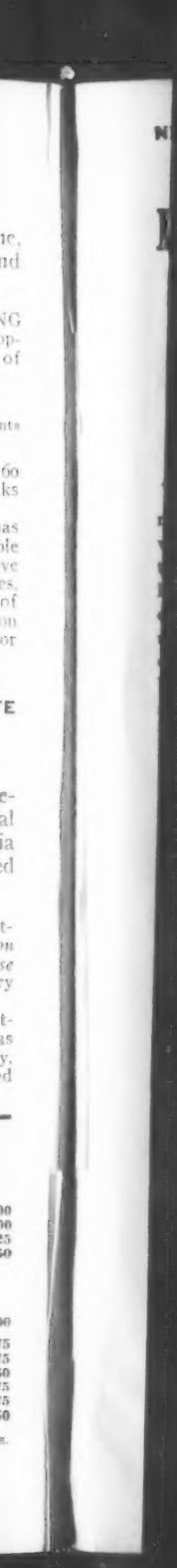

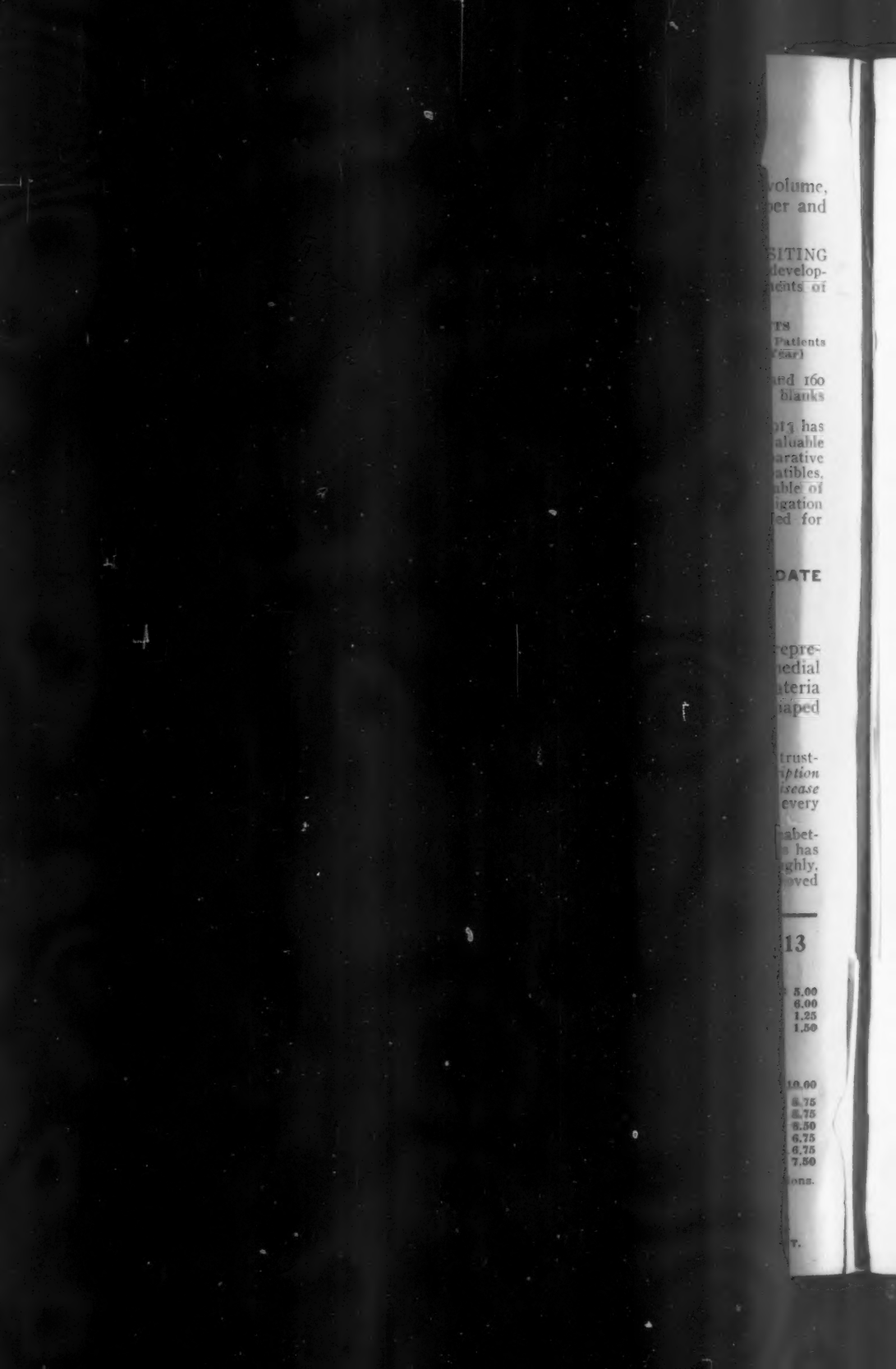

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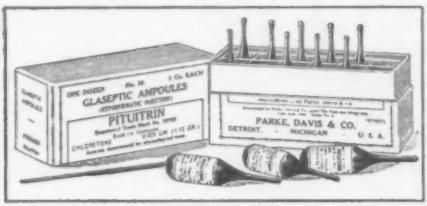

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